A study of pain and mortality: the role of lifestyle, health, social and psychological factors

Diane Smith

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Arthritis Research UK Primary Care Centre

Abstract

Background

Moderate to severe chronic pain affects one in five of adults. The prevalence and impact of pain increase with age. Pain may increase the risk of mortality but the relationship is not clear.

Aims

To test the hypothesis that pain increases the risk of mortality, to test if the relationship was dependent on pain classification and identify mediators and moderators of the relationship.

Methods

A systematic review and meta-analysis evaluated existing evidence. Survival analyses (Cox's proportional hazard modelling and a novel technique to assess mediation within survival models) were conducted on two large population studies of adults aged ≥50 years; the English Longitudinal Study of Ageing (ELSA) (n=6324) and the North Staffordshire Osteoarthritis Project (NorStOP) (n=10985). Lifestyle, health, social and psychological factors were tested as potential mediators. Sex and comorbidity were tested as moderators.

Results

In the systematic review pooled analysis from 7 studies revealed a modest but non-significant risk of mortality for people with chronic pain (Mortality Rate Ratio 1.14, 95%CI

(0.95, 1.37)). In survival analyses the relationship with mortality was influenced by pain classification: pain that was troubling (1.29 (1.12, 1.49)) or that interfered with daily activities (1.88 (1.54, 2.29)) was associated with an increased risk of mortality while reporting any pain was not (1.06 (0.95, 1.19)).

The strongest mediators in ELSA that were replicated in NorStOP were functional limitation (Hazard Ratio 1.31; 95%CI (1.20, 1.39)), physical inactivity (1.14 (1.10, 1.20)) and poor self-rated health (1.32 (1.23, 1.41)). Sex and comorbidity moderated the extent of some mediating pathways (e.g. depression) but the findings were inconsistent between datasets.

Conclusion

Specific opportunities to reduce mortality risk for people with pain were identified. At a population level, mortality risk for people with pain could be reduced by the effective management of pain and its impact.

Contents

Abstract i
List of tables ix
List of figures xii
List of abbreviations xiv
Acknowledgements xviii
Chapter One. Background 1
1.1 Introduction 1
1.2 What is pain? 1
1.3 Theories of pain 2
1.3.1 Early theories of pain 2
1.3.2 The Gate Control Theory 4
1.3.3 The Neuromatrix Theory 6
1.4 Pain phenotypes 10
1.4.1 Pain duration 11
1.4.2 Location 13
1.5 Epidemiology of pain 17
1.5.1 Prevalence of pain 18
1.5.2 The distribution of pain by age 20
1.5.3 Distribution of the prevalence of pain by sex 20
1.5.4 Distribution of pain by socio-economic status 22
1.5.5 Economic consequences of pain 23
1.6 Impact of pain – a focus on mortality 25
1.6.1 Studies of pain and mortality 26
1.7 Key messages 29
Chapter Two. Chronic pain and mortality: a systematic review and meta-analysis 30
2.1 Chapter summary 30
2.2 Introduction 30
2.2.1 Advantages and disadvantages of systematic reviews 31
2.3 Aim 32
2.4 Objectives 32

2.5 Methods 33
2.5.1 Phase 1: Search strategy and identification of studies (objective 1) 33
2.5.2 Phase 2. Study selection (objective 1) 34
2.5.3 Phase 3: Data extraction and quality assessment (objective 2) 35
2.5.4 Phase 4: Data extraction and analysis (objective 3) 41
2.6 Results 44
2.6.1 Identification of studies 44
2.6.2 Quality assessment 51
2.6.3 Study findings 53
2.6.4 Evidence synthesis: meta-analysis 54
2.6.5 Evidence synthesis: narrative review of potential sources of heterogeneity 63
2.7 Discussion 68
2.7.1 Summary of findings 68
2.7.2 Differences between studies 69
2.7.3 Strengths and limitations 74
2.7.4 Implications for research 75
2.8 Potential pathways from pain to mortality 76
2.8.1 Lifestyle factors 76
2.8.2 Health factors 80
2.8.3 Social factors 85
2.8.4 Psychological factors 87
2.9 Potential moderators of a relationship between pain and mortality 93
2.9.1 Sex 94
2.9.2 Comorbidity 95
2.10 Key messages 96
Chapter Three. Aims and objectives 97
3.1 Aims 97
3.2 Specific objectives 97
3.3 Thesis content 98
Chapter Four. Data sources 100
4.1 Introduction 100
4.2 Aims 101
4.3 Preparation and analysis of datasets 102

4.4 Study design 103
4.4.1 The English Longitudinal Study of Ageing (ELSA) 103
4.4.2 The North Staffordshire Osteoarthritis Project (NorStOP) 108
4.5 Participant flow 113
4.5.1 ELSA 113
4.5.2 NorStOP 119
4.6 Missing data 121
4.6.1 Introduction 121
4.6.2 Aim 124
4.6.3 Methods 124
4.6.4 Results 125
4.6.5 Implications 125
4.7 Power analysis 126
4.7.1 Introduction 126
4.7.2 Aim 127
4.7.3 Methods 128
4.7.4 Results from ELSA 129
4.7.5 Allostatic load and frailty 129
4.7.6 Results from NorStOP 131
4.7.7 Implications 131
4.8 Comparisons between samples 132
4.8.1 Introduction 132
4.8.2 Aim 133
4.8.3 Methods 133
4.8.4 Results from ELSA 133
4.8.5 Allostatic load 135
4.8.6 Frailty 136
4.8.7 Results from NorStOP 137
4.8.8 Implications 139
4.9 Comparison of the ELSA and NorStOP baseline complete case samples with national statistics 140
4.9.1 Introduction 140
4.9.2 Aim 141
4.9.3 Methods 141

4.9.4 ELSA....141
4.9.5 NorStOP....142
4.9.6 Implications....143
4.10 Discussion....144
4.10.1 Summary of findings....144
4.10.2 Implications....145
4.11 Key messages....147
Chapter Five. The influence of pain phenotype on mortality....148
5.1 Introduction....148
5.2 Aims....148
5.3 Methods....149
5.3.1 Survival analysis....149
5.3.2 Applying survival analysis to ELSA and NorStOP data....155
5.4 Exposures and outcomes....156
5.4.1 The English Longitudinal Study of Ageing (ELSA)....156
5.4.2 The North Staffordshire Osteoarthritis Project (NorStOP)....160
5.5 Statistical analysis....165
5.5.1 Sample characteristics....165
5.5.2 Survival analysis....166
5.5.3 Weighting....167
5.5.4 Assumption testing....169
5.6 Results of the descriptive analysis....170
5.6.1 The ELSA complete case sample....170
5.6.2 The NorStOP complete case sample....172
5.7 Results of the survival analysis....176
5.7.1 Often troubled with pain (ELSA) and mortality....176
5.7.2 Severity of pain (ELSA)....177
5.7.3 Any pain (NorStOP)....179
5.7.4 ACR WP (NorStOP)....181
5.7.5 Manchester WP (NorStOP)....183
5.7.6 Number of pain sites (NorStOP)....184
5.7.7 Pain interference (NorStOP)....185
5.7.8 Cause-specific mortality (ELSA only)....191

5.8 Discussion 199
5.8.1 Summary of results 199
5.8.2 Methodological considerations 200
5.8.3 Comparison with other studies 202
5.8.4 Strengths and limitations 209
5.8.5 Implications for further research 210
5.9 Key messages 211
Chapter Six. Mechanisms of association between pain and mortality 212
6.1 Introduction 212
6.2 Aims 212
6.3 Methods 213
6.3.1 Mediation 213
6.3.2 Mediation analysis 215
6.3.3 Measurement of the proposed mediators in the ELSA and NorStOP datasets 221
6.3.4 Mediation analysis within the ELSA and NorStOP samples 230
6.3.5 Moderation 231
6.3.6 Moderation analysis 232
6.3.7 Combining mediation and moderation 232
6.3.8 Measurement of the proposed moderators in the ELSA and NorStOP datasets 234
6.4 Results of the mediation analyses 236
6.4.1 Lifestyle factors 236
6.4.2 Health factors 241
6.4.3 Social factors 241
6.4.4 Psychological factors 241
6.5 Results of the moderation analyses 241
6.5.1 Stratification by sex 241
6.5.2 Stratification by comorbidity 248
6.6 Allostatic load and Frailty (ELSA only) 256
6.6.1 Mediation by allostatic load 256
6.6.2 Mediation by frailty 256
6.7 Discussion 259
6.7.1 Summary of findings 259
6.7.2 Interpretation of findings 259

6.7.3 Interventons to reduce mortality risk 268
6.7.4 Comparison with other studies 268
6.7.5 Methodological considerations 269
6.7.6 Strengths and limitations 275
6.7.7 Implications for research and practice 277
6.8 Key messages 277
Chapter Seven. Discussion 278
7.1 Thesis summary 278
7.2 General discussion 278
7.2.1 Summary of findings 278
7.3 Implications for research 279
7.3.1 Mediation analysis 279
7.3.2 Mediation analysis within survival analysis 281
7.3.3 Secondary data analysis 282
7.3.4 Generalisability of findings 284
7.4 Implications for practice 285
7.4.1 Interventions to reduce mortality risk 285
7.4.2 Obstacles to effective pain management 286
7.5 Concluding messages 287
List of publications and presentations 289
References 290
Appendix I - Full search strategy 323
Appendix II - Quality in Prognosis Studies (QUIPS) 336
Appendix III - Missing data correlations 344
Appendix IV - Weighted survival analyses 510
Appendix V - Schoenfeld tests and residual plots 515
Appendix VI - Survival models with interaction terms 547
Appendix VII - Measurement of the proposed mediators in the ELSA and NorStOP datasets 549
Appendix VIII - R code for mediation in survival analysis 565
Appendix IX – Systematic review paper 568

List of tables

Table 1.1 Prevalence figures for common regional pain sites in adults (reproduced from Henschke et al., 2015) 14
Table 1.2 Results of PubMed search for reviews of the prevalence and impact of pain from 2010 to 2015 18
Table 1.3 Estimated total annual financial costs of chronic pain conditions for selected countries 24
Table 2.1 Summary of the papers included in the systematic review 47
Table 2.2 Summary of agreed level of bias between the two reviewers and percentage agreement for each potential area of bias and overall Kappa for each study .52
Table 2.3 Summary of main sources of heterogeneity between the included studies in the systematic review 64
Table 4.1 The role of ELSA variables in the survival analysis (Chapter Five) and the mediation and moderation analyses (Chapter Six) 107
Table 4.2 The role of NorStOP variables in the survival analysis (Chapter Five) and mediation and moderation analyses (Chapter Six) 113
Table 4.3 The anticipated and achieved Wave 1 ELSA sample stratified by age and sex..114
Table 4.4 Power to detect expected hazard ratios per sample size in the achieved samples from the ELSA dataset; α=0.05 129
Table 4.5 Power to detect expected hazard ratios per sample size in the achieved samples from the NorStOP dataset; α=0.05 131
Table 4.6 Comparison of participants with complete data to those with missing mediator data from ELSA 134
Table 4.7 The number and proportion of participants with complete allostatic load data in ELSA at baseline and those with missing data 135
Table 4.8 The number and proportion of participants with complete frailty data in ELSA at baseline to those with missing data 137
Table 4.9 Comparison of participants with complete data to those with missing mediator data in NorStOP 138
Table 4.10 Comparison of the ELSA complete case sample (n=6324) with National statistics according to age group 142
Table 4.11 Comparison of the ELSA complete case sample (n=6324) with National statistics according to sex distribution per age group 142
Table 4.12 Comparison of the NorStOP complete case sample (n=10985) with National statistics according to age group 143
Table 4.13 Comparison of the NorStOP complete case sample (n=10985) with National statistics according to sex distribution per age group 143
Table 5.1 Pain phenotypes tested for their relationship with mortality 166

Table 5.2 Characteristics of the ELSA complete case sample overall and stratified by vital status 170
Table 5.3 Descriptive characteristics of the total NorStOP complete case sample and stratified according to mortality status 173
Table 5.4 Risk of all-cause mortality in the ELSA complete case sample according to pain phenotype (n=6324) 180
Table 5.5 Risk of all-cause mortality in the NorStOP complete case sample according to pain phenotype (n=10985) 186
Table 5.6 Risk of all-cause mortality in the NorStOP complete case sample according to pain interference in the first year of follow up (0-365 days) 189
Table 5.7 Risk of all-cause mortality in the NorStOP complete case sample according to pain interference after the first year of follow up (365 to 3483 days) 190
Table 5.8 Risk of cancer mortality in the ELSA complete case sample according to pain phenotype (n=6324) 193
Table 5.9 Risk of cardiovascular disease mortality in the ELSA complete case sample according to pain phenotype (n=6324) 193
Table 5.10 Risk of respiratory disease mortality in the ELSA complete case sample according to pain phenotype (n=6324) 197
Table 5.11 Risk of other mortality in the ELSA complete case sample according to pain phenotype (n=6324) 197
Table 5.12 Risk of unknown mortality in the ELSA complete case sample according to pain phenotype (n=6324) 198
Table 5.13 Cross tabulation of the number of pain sites and pain interference categories presenting the proportion of those who died in the NorStOP complete case sample (n= 10953) * 207
Table 6.1 Measures of the proposed mediating lifestyle factors in the ELSA and NorStOP datasets 222
Table 6.2 Measures of the proposed mediating health factors in the ELSA and NorStOP datasets 224
Table 6.3 Measures of the proposed mediating social factors in the ELSA and NorStOP datasets 227
Table 6.4 Measures of the proposed mediating psychological factors in the ELSA and NorStOP datasets 228
Table 6.5 Pathways between 'often troubled with pain' and mortality via lifestyle, health, social and psychological factors for the for the ELSA complete case sample (n=6324): Direct, indirect and total effects. 237
Table 6.6 Pathways between 'any pain' and mortality via lifestyle, health, social and psychological factors for the NorStOP complete case baseline sample (n=10985): Direct, indirect and total effects 239

Table 6.7 Pathways between 'often troubled with pain' and mortality via lifestyle, health, social and psychological factors in the ELSA complete case sample (n=6324) stratified by sex: Direct, indirect and total effects. 242
Table 6.8 Pathways between 'any pain' and mortality via lifestyle, health, social and psychological factors for the NorStOP complete case baseline sample (n=10985): Direct, indirect and total effects stratified by sex. 245
Table 6.9 Pathways between 'often troubled with pain' and mortality via lifestyle, health, social and psychological factors in the ELSA complete case sample (n=6324) stratified by comorbidity: Direct, indirect and total effects. 250
Table 6.10 Pathways between 'any pain' and mortality via lifestyle, health, social and psychological factors for the NorStOP complete case baseline sample (n=10985): Direct, indirect and total effects stratified by comorbidity.....253
Table 6.11 Pathways between 'often troubled with pain' and mortality via allostatic load in ELSA: Direct, indirect and total effects. 257
Table 6.12 Pathways between 'often troubled with pain' and mortality via frailty in ELSA: Direct, indirect and total effects. 258
Table 6.13 Significant mediating factors in each sample from each dataset 260

List of figures

Figure 1.1 Circuit diagram of the Gate Control Theory of pain perception (Melzack and Wall, 1965) 6
Figure 1.2 Factors that contribute to the pattern of activity gated by the body-self neuromatrix (Melzack and Katz, 2004) 7
Figure 1.3 The biopsychosocial model of health and illness....9
Figure 1.4 The prevalence of widespread pain (WP) in the North Staffordshire Osteoarthritis Project (NorStOP) stratified by age and sex n=7878. (Thomas et al., 2004)....21
Figure 2.1 Flow chart of the selection of papers for the systematic review 46
Figure 2.2 Forest plot of the of the association between chronic pain and all-cause mortality in identified studies (effect sizes are MRR only) 55
Figure 2.3 Forest plot of the association between chronic widespread pain and all-cause mortality in identified studies (effect sizes are MRR only) 56
Figure 2.4 Forest plot of the association between chronic pain and cancer mortality in identified studies (MRR only)....57
Figure 2.5 Forest plot of the association between chronic widespread pain and cancer mortality in identified studies (MRR only) 58
Figure 2.6 Forest plot of the association between chronic pain and cardiovascular disease mortality in identified studies (MRR only) 59
Figure 2.7 Forest plot of the association between chronic widespread pain and cardiovascular disease mortality in identified studies (MRR only)....60
Figure 2.8 Forest plot of the association between chronic pain and respiratory disease mortality in identified studies (MRR only) 61
Figure 2.9 Forest plot of the association between chronic widespread pain and respiratory disease mortality in identified studies (MRR only) 62
Figure 4.1 Flow diagram of Chapter Four 102
Figure 4.2 Number of participants at each wave of ELSA (Steptoe et al., 2012)....116
Figure 4.3 Number and proportion of participants with missing data at each stage of ELSA 118
Figure 4.4 Flowchart of baseline response in NorStOP 119
Figure 4.5 Number and proportion of participants with missing data at each stage of NorStOP....120
Figure 5.1 Representation of 7 participants with staggered entry and follow up over 10 years in survival analysis (adapted from Cox and Oakes, 1984) 150
Figure 5.2 Example of a Kaplan Meier survival curve 152
Figure 5.3 NorStOP Manikin....161
Figure 5.4 NorStOP template for calculating pain sites/widespread pain 163

Figure 5.5 Survival probability over 92 months for often troubled with pain and those not often troubled by pain; Kaplan Meier plots in the ELSA complete case sample (n=6324) 177
Figure 5.6 Survival probability over 92 months for levels of pain severity; Kaplan Meier estimates in the ELSA complete case sample (n=6324).....178
Figure 5.7 Survival probability over 10 years for any pain and those with no pain; Kaplan Meier plots in the NorStOP complete case sample (n=10985).....181
Figure 5.8 Survival probability over 10 years for American College of Rheumatology Widespread Pain (ACR WP) criteria; Kaplan Meier estimates in the NorStOP complete case sample (n=10953) 182
Figure 5.9 Survival probability over 10 years for Manchester Widespread Pain criteria (Manchester WP); Kaplan Meier estimates in the NorStOP complete case sample (n=10953).....183
Figure 5.10 Survival probability over 10 years for number of pain sites; Kaplan Meier estimates in the NorStOP complete case sample (n=10953) 184
Figure 5.11 Survival probability over 10 years for pain interference; Kaplan Meier estimates in the NorStOP complete case sample (n=10985) 187
Figure 6.1 Simple mediation model 214
Figure 6.2 Simple moderation model 232
Figure 6.3 Moderation and mediation model.....234

List of abbreviations

Acceptance and Commitment Therapy	ACT
Activities of Daily Living	ADL
Adjusted Odds Ratio	AOR
Ageing Perceptions Questionnaire	APQ
American College of Rheumatology	ACR
Body Mass Index	BMI
Cardiovascular disease	CVD
Centre for Epidemiologic Studies Depression scale	CESD
Certificate of Secondary Education	CSE
Chinese Health, Aging and Retirement Longitudinal Study	CHARLS
Chronic Obstructive Pulmonary Disease	COPD
Chronic Pain	CP
Chronic Widespread Pain	CWP
Computer Aided Personal Interviewing	CAPI
Confidence Interval	CI
Control, Autonomy, Self-realisation, Pleasure scale	CASP
Deoxyribonucleic acid	DNA
Diane Smith	DS
Disability Adjusted Life Years	DALY
English Longitudinal Study of Ageing	ELSA
Fibromyalgia	FM
Functional Limitations Profile	FLP
General Certificate of Education	GCE
General Medical Council	GMC
General Practice Research Database	GPRD
General Practitioner	GP

General Register Office	GRO
Generalised Linear Modelling	GLM
Generalised Structural Equation Modelling	GSEM
Global Burden of Diseases, Injuries and Risk Factors	GBD
Great British Pound	GBP
Gross Domestic Product	GDP
Hazard Ratio	HR
Health and Retirement Survey	HRS
Health and Social Care Information Centre	HSCIC
Health Related Quality of Life	HRQoL
Health Surveys for England	HSE
High Density Lipoprotein	HDL
Hospital Anxiety and Depression Scale	HADS
Hospital Episode Statistics	HES
Hypothalamic Pituitary Adrenal	HPA
Illness Perception Questionnaire (Revised)	IPQ-R
Indonesia Family Life Survey	IFLS
Instrumental Activities of Daily Living	IADL
Insulin-like Growth Factor	IGF
Inter Quartile Range	IQR
Interleukin	IL
International Association for the Study of Pain	IASP
International Classification of Diseases and Related health problems	ICD
International Classification of Functioning, Disability and Health	ICF
Irish Longitudinal Study on Ageing	TILDA
Japanese Study on Aging and Retirement	J-STAR
Jo Jordan	JJ

John McBeth	JM
Karlson Holm Breen	KHB
Keele Assessment of Participation	KAP
Korean Longitudinal Study on Ageing	KLoSA
Longitudinal Aging Study in India	LASI
Low Density Lipoprotein	LDL
Manchester Chronic Widespread Pain	CWP-M
Medical Certificate of Cause of Death	MCCD
Medical Outcomes Study	MOS
Meta-analysis of Observational Studies in Epidemiology	MOOSE
Mexican Health and Aging Study	MHAS
Missing at Random	MAR
Missing Completely At Random	MCAR
Missing Not At Random	MNAR
Mortality Rate Ratio	MRR
Multiple Imputation	MI
National Centre for Social Research	NatCen
National Health Service Central Register	NHSCR
National Vocational Qualification	NVQ
North Staffordshire Osteoarthritis Project	NorStOP
Odds Ratio	OR
Office of National Statistics	ONS
Postcode Address File	PAF
Quality in Prognosis Studies tool	QUIPs
Quality of Life	QoL
Research Ethics Committee	REC
Ross Wilkie	RW

Self-Regulatory Model	SRM
Short Form -12	SF-12
Short Form -36	SF-36
Sickness Impact Profile	SIP
Standardised Mortality Ratio	SMR
Statistical Package for the Social Sciences	SPSS
Strengthening of Reporting of Observational Studies	STROBE
Structural Equation Modelling	SEM
Study on Global Aging and Adult Health	SAGE
Survey of Health, Ageing and Retirement in Europe	SHARE
Symptom Severity	SS
United Kingdom	UK
Widespread Pain Index	WPI
Widespread Pain	WP
World Health Organisation	WHO
Years Lived with Disability	YLD
Years of Life Lost	YLL

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Chapter One. Background

1.1 Introduction

Pain has a major impact on the individual and society (Woolf, Erwin, & March, 2012) which is recognised by the World Health Organisation and the United Nations as a global problem that is expected to escalate as life expectancy increases and the world's population ages (Woolf & Pfleger, 2003). The impact of pain is broad and includes reduced quality of life, disability, lost workdays and demands on healthcare (Soldato et al., 2007; Tüzün, 2007; Woolf, Erwin & March., 2012). Pain can be considered as a condition in its own right as it can persist even after a precipitating injury or condition has healed (Siddall & Cousins, 2004). Irrespective of cause, the high prevalence of pain and its subsequent impact warrant the recognition of pain as an important public health problem (Blyth, Van Der Windt, & Croft, 2015; Croft, Blyth, & Van Der Windt, 2010).

1.2 What is pain?

The definition of pain proposed by the International Association for the Study of Pain (IASP) (i.e. "pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey & Bogduk, 1994)) is highly cited but lacks the detail necessary to characterise what is a complex phenomenon. Pain is essential for survival; when the nervous system responds to the detection of potentially damaging stimuli behavioural responses are initiated to protect against further damage (Kopf & Patel, 2010). However pain is more than a sensation in response to an external stimulus. It is a complex interaction of physical and psychological factors (Serpell, 2005); the neurophysiological response to a painful

stimulus is influenced by a complex combination of genetic, environmental, cultural, socioeconomic and psychological factors (Brooks, 2005). This complexity and the uniqueness of the pain experience to the individual makes defining pain challenging. Meaningful theories of pain have evolved which provide the basis for pain phenotypes, an understanding of pain mechanisms and the resulting impact for the individual.

1.3 Theories of pain

1.3.1 Early theories of pain

In 1664, Descartes' theory of pain was the first time a link between mind and body had been proposed to explain the experience of pain. Prior to this, early theories attributed pain to religious influences (e.g. punishment or a test from god, or the entry of evil spirits into the body through an injury), an imbalance in vital fluids, or considered it to be an emotion or sensation experienced in the heart (Main, Sullivan, & Watson, 2007). Descartes' theory proposed that pain was a perception that existed in the brain and was separate to the neural phenomenon of sensory transduction conducted through nerves which he described as hollow tubes that conveyed both sensory and motor information (Moayedi & Davis, 2013). A sensory cue would 'tug' on a tube which would open a gate between the tube and the brain allowing "animal spirits" to flow through them and within the muscles to initiate movement (Moayedi & Davis, 2013). A pervasive assumption from this theory was that the amount of pain was directly related to the amount of tissue damage. The theory also implied pain travelled in one direction only and that pain would cease if the stimulus was stopped (Main et al., 2007).

Descartes' concept of a pain pathway linking peripheral body parts to the brain provided the basis for the development of the Specificity Theory by Charles Bell in 1811 (Moayedi

& Davis, 2013). Bell suggested that the brain was a heterogeneous structure and that nerves consisted of heterogeneous bundles of neurons which had specialized functions (Moayedi & Davis, 2013). Both Descartes and Bell's theories suggested a relatively simple relationship between tissue damage and pain however these could not explain phenomena such as phantom limb pain (where pain is experienced in a limb that has been amputated), dissociations between injuries and pain like those observed in soldiers in the Second World War (where severe wounds resulted in little reported pain) (Beecher, 1946), pain in the absence of tissue damage or the persistence of pain beyond tissue-healing time (Main et al., 2007).

Other theories began to develop ideas on the mechanism between tissue damage and the perception of pain by the individual. Examples were the Intensity Theory (Erb, 1874), which proposed that pain occurs in any sensory system if the stimulus is of sufficient intensity (i.e. there are no distinct pathways), and the Pattern Theory (Nafe, 1929), where a specific and particular pattern of activity of different neurons determines the stimulus type and intensity of a sensation (Perl, 2007). Despite these alternative theories, the Specificity Theory of pain became dominant; posing different types of neurons for different types of stimuli and proposed a dedicated pain pathway (Moayedi & Davis, 2013). This theory gained support from the work of von Frey between 1894 and 1896 who proposed four somatosensory modalities: cold, heat, pain and touch. In 1947, Sherrington recognised that neurons responded to specific stimuli including von Frey's four modalities and proposed the framework for nociception (described below) (Moayedi & Davis, 2013) which was incorporated into the ensuing dominant theory; the Gate Control Theory of pain (Melzack & Wall, 1965).

1.3.2 The Gate Control Theory

The Gate Control Theory (Melzack & Wall, 1965) (Figure 1.1) provided a framework to view pain as a psychophysiological phenomenon; a combination of mental and biological processes. The Gate Control Theory outlined mechanisms for the transmission and modulation of nociceptive (pain) signals which, for the first time, highlighted the potential role of psychological and social/environmental factors in the overall pain experience (Main et al., 2007).

Nociception

Nociception is the process of transduction and transmission of noxious stimuli via a pain pathway to the brain (Steeds, 2009). Noxious stimuli are detected by nociceptors which are receptors in tissues that respond to painful stimuli (Steeds, 2009). Nociceptors are the free nerve endings of nerve fibres of which there are two main types; fast conducting A-delta fibres and slower conducting C fibres (Steeds, 2009). A-delta fibres are involved in the rapid localisation of pain and withdrawal from the stimulus thus having a protective effect. They are high threshold receptors which respond to thermal and mechanical stimuli and are thinly myelinated (Serpell, 2005). Myelination refers to the coating of the axons of nerve fibres with myelin which acts to increase the speed of conductivity of nerve impulses by reducing leakage of the electrical current and causing the signal to jump along sections of the nerve fibre between breaks in the myelin (Widmaier, Raff, & Strang, 2008). C fibres are involved in delayed pain sensation in response to tissue injury and elicit processes which act to protect and heal the damaged area. They are unmyelinated, slow conducting and respond to mechanical, thermal and chemical stimuli. About 15% of C fibres have ‘silent’ or ‘sleeping’ nociceptors present in the skin and

viscera which become active under inflammatory conditions only (Serpell, 2005). C fibres travel alongside larger myelinated A-beta fibres which are involved in the processing of non-painful stimuli like touch and vibration (Steeds, 2009).

Pain modulation

Pain modulation refers to the regulation of the intensity of pain perception by other factors (Ossipov, Dussor, & Porreca, 2010). Modulation occurs when a 'gate' located in the substantia gelatinosa in the dorsal horn of the spinal cord either 'opens' or 'closes' in response to collective inputs leading to increased or decreased pain perception (Melzack & Wall, 1965). This gating mechanism is influenced by the relative amount of activity in the nerve fibres and by nerve impulses that descend from the brain. For example, activity of larger A-beta fibres (L in Figure 1.1) (associated with non-painful stimuli) act to close the gate whereas activity by the smaller A-delta and C-fibres (S in Figure 1.1) (associated with painful stimuli) open the gate (Melzack, 1993). Selective cognitive processes are activated by the central control trigger; a system of large fast conducting fibres, which influence modulation via the gating system. This 'central control' refers to processes in the brain involved in the identification, evaluation and modulation of input before the activation of the action system (neural areas which control the experience of and behaviours associated with pain) by the transmission (T) cells. The action system is activated once the spinal cord transmission exceeds a certain level (Melzack, 1993) (Figure 1.1).

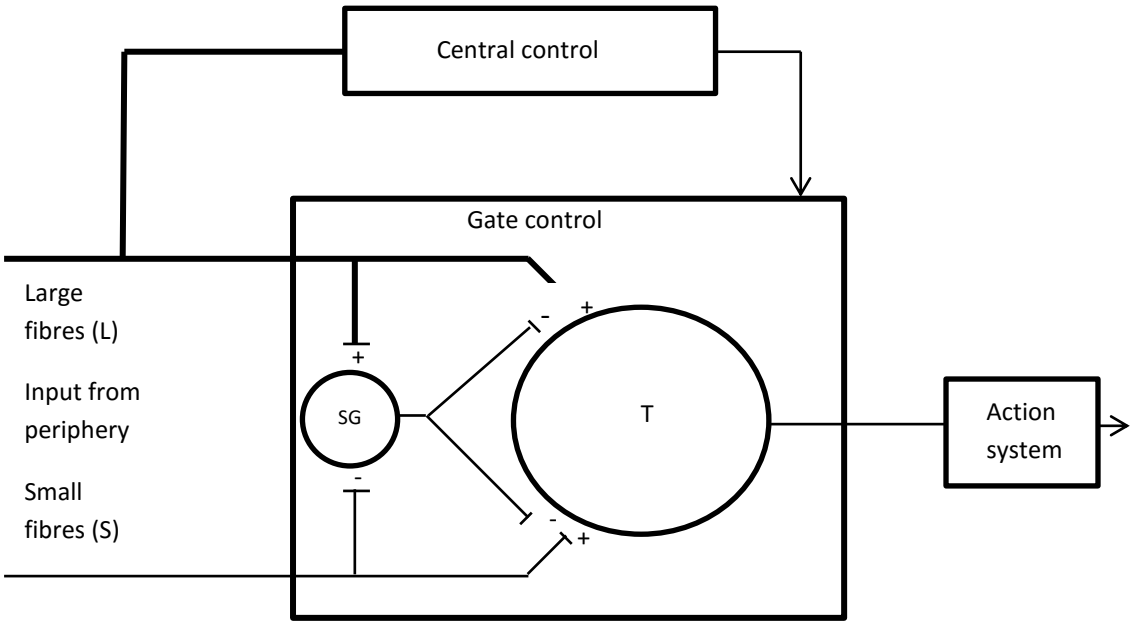


Figure 1.1 Circuit diagram of the Gate Control Theory of pain perception (Melzack and Wall, 1965)

Large diameter fibres (L) and small diameter fibres (S) project to the substantia gelatinosa (SG) and the first central transmission (T) cells. The SG exerts an inhibitory effect on the afferent fibre terminals which is increased by activity of the L fibres and decreased by activity of the S fibres. The line running from the large fibres to the central control mechanisms represents the central control trigger. The central control mechanisms then project back to the gate control system. The T cells project to the action system (Melzack and Wall, 1965)

The Gate Control Theory was further revised in 1999 to acknowledge that different neural systems were responsible for the motivational, affective and cognitive aspects of the pain experience (Main et al., 2007). This emphasised the dynamic role of the brain/central neural mechanisms in pain processes with psychological factors playing an integral part (Melzack, 1999).

1.3.3 The Neuromatrix Theory

The emphasis on central neural mechanisms posited by the Gate Control Theory and the integration of pain research and psychophysiological research culminated in the Neuromatrix Theory (Melzack, 1999). This coincided with increasing interest in chronic pain and disability, and introduced a theoretical framework for their development (Main

et al., 2007). The Neuromatrix theory proposed a characteristic pattern of nerve impulses or “neurosignature” which is generated by a widely distributed neural network and may be triggered by or occurs independently of sensory inputs (Melzack and Katz in Hadjistavropoulos & Craig, 2004). The neuromatrix is genetically determined but is modified by sensory experience and its output pattern is determined by multiple influences (Melzack, 1999) (Figure 1.2).

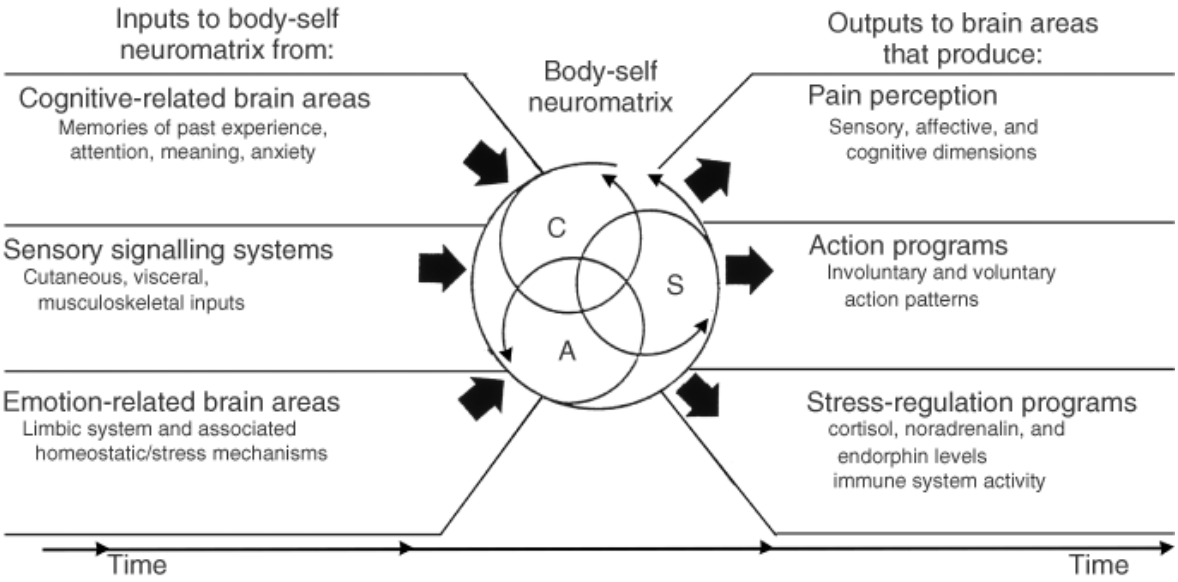


Figure 1.2 Factors that contribute to the pattern of activity gated by the body-self neuromatrix (Melzack and Katz, 2004)

The neuromatrix is comprised of sensory (S), affective (A), and cognitive neuromodules (C). Combinations of input factors influence the patterns of activity of these neuromodules which results in output patterns representing the multidimensional experience of pain (Melzack and Katz, 2004).

Different areas of the brain play a more or less active role depending on the interaction between factors (e.g. cognition, mood, injury) influencing pain perception. At present, there is no clear consensus over which areas of the brain make up the pain matrix (Tracey & Mantyh, 2007). Neuroimaging has enabled the identification of neural activity in pain

processing but pain experience is determined by the interaction of different brain regions. An individual neural 'pain signature' is a more useful way to describe the subjective experience of pain rather than trying to explain it in terms of a rigid neuroanatomical pain matrix (Tracey & Mantyh, 2007). The Neuromatrix Theory aligned with the biopsychosocial approach to health and illness and highlighted the multidimensional (biological, psychological and social/environmental) aspects of pain perception which also determine the extent and characteristics of its impact.

The understanding of the experience of pain will continue to develop. The theories of pain, through identifying the multifactorial influences indicate that different approaches (e.g. analgesia, cognitive behavioural approaches) may be applied to reduce the experience of pain by individuals. Pain should be considered to be a complex, subjective multifactorial experience similar to other chronic health conditions. Symptoms and illnesses may originate from a biological source but the chronicity of a condition and the development of incapacity can often be the result of psychosocial factors (Waddell, 2006). Theories of pain have linked with disability frameworks to provide an understanding of how its impact occurs but perhaps more importantly to identify potential targets to reduce it. More recent models of disability embody a biopsychosocial approach to health and illness, first proposed by Engel in 1977. The biopsychosocial model posits illness and the impact of health conditions as a complex interaction of biological (e.g. injury), psychological (e.g. depression) and social factors (e.g. living alone) (Engel, 1977) (Figure 1.3). The distinction between disease; "an objective biological event involving the disruption of specific body structures or organ systems caused by anatomical, pathological or physiological changes" and illness; "a subjective experience or

self-attribution that a disease is present" can be likened to the distinction between nociception (objective processes) and pain (subjective experience) (Gatchel, Peng, Peters, Fuchs, & Turk, 2007).

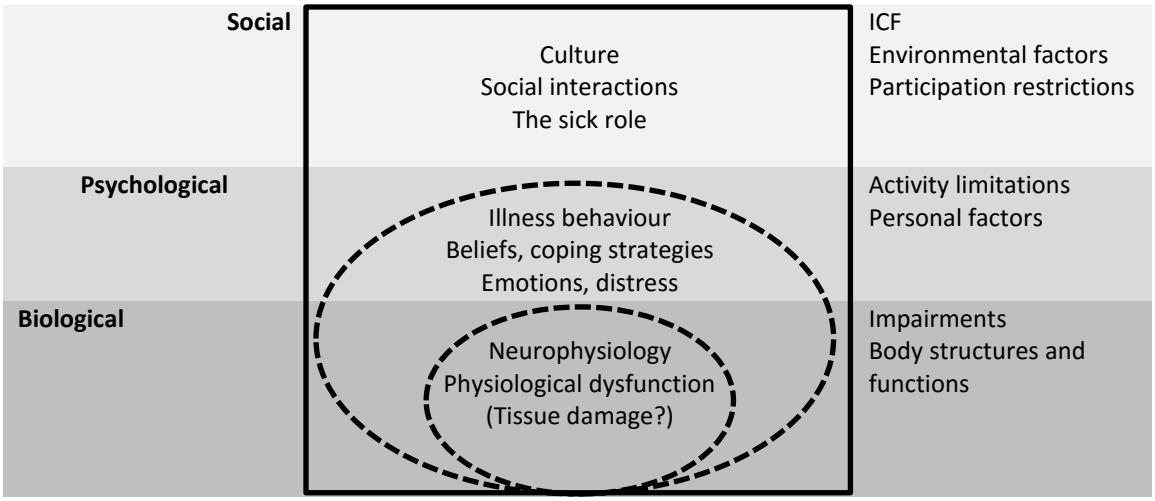


Figure 1.3 The biopsychosocial model of health and illness

The biopsychosocial model of health and illness reproduced from Waddell (2006) with corresponding International Classification of Functioning, Disability and Health (ICF) components (Waddell, 2006).

The experience of pain is unique to the individual. A range of psychological and environmental factors interact with physical pathology to influence the experiences of pain and an individual's responses to it. The emergence of the biopsychosocial model has driven an interdisciplinary approach to pain management (Gatchel et al., 2007) and provides the basis for the World Health Organisation International Classification of Functioning, Disability and Health (ICF). The ICF is widely accepted as the framework for disability and rehabilitation and considers functioning and disability as a dynamic interaction between an individual's health condition, personal/psychological factors and social/contextual factors (Waddell, 2006). Understanding how pain, lifestyle, health,

social and psychological factors link together can help to focus and direct what health and social care should target to reduce the burden of pain on individuals.

The evolving theories, outlined above, have provided a platform for our understanding of pain and its impact and broad frameworks that drive the current approaches to management by multidisciplinary health teams. The current challenge of unpicking the 'pain signature', identifying how biological, psychological and environmental factors interact and further refinement of the theories of pain would benefit from epidemiological studies which can identify exposures and potential mechanisms of the pain experience and its impact. Focusing on specific phenotypes provides a basis for the epidemiology of pain; these are often how pain is characterised in clinical practice and research and provide a focus for identifying natural history (incidence and prognosis), predictors and pertinent treatment approaches.

1.4 Pain phenotypes

Phenotypes are the appearances, signs and symptoms of disease and are dynamic; influenced by the underlying genotype, the environment and interactions between them (Wojczynski & Tiwari, 2008). Pain phenotypes overlap and can be viewed as a continuous spectrum, with common acute regional pain problems such as minor headaches at the lower end of the spectrum and chronic pain problems such as chronic widespread pain (CWP) including fibromyalgia at the other (Croft et al., 2010). Pain phenotypes are routinely characterised using duration and anatomical location.

1.4.1 Pain duration

Pain defined by duration can be classed as acute (less than three months) or chronic (three months or more). Acute pain typically occurs in response to a noxious stimulus which does not overwhelm the body's responses and resolves in days or weeks (Loeser & Melzack, 1999). It has a protective function, either by initiating the withdrawal reflex from a noxious stimulus or by heightening sensory sensitivity following tissue damage which aids healing of the damaged area by discouraging movement or physical contact and reduces the risk of further damage (Woolf, 2010).

Chronic pain is commonly defined as that which lasts beyond normal healing time, usually taken to be beyond three months (Merskey & Bogduk, 1994). Pain is often considered as a symptom of underlying disease or injury (Blyth et al., 2015). However chronic pain should be regarded as a health condition in its own right because, as the theories of pain indicate, it has its own pathology, symptoms and signs (e.g. altered receptor function, mood dysfunction, social disruption) (Siddall & Cousins, 2004). Pain can persist beyond its precipitating cause (i.e. beyond what we would regard as acute pain) and it may not be possible to address the underlying pathology (Siddall & Cousins, 2004). Pain can also occur without an obvious pathological reason, for example in fibromyalgia patients an underlying cause is often difficult to determine (Bergman, 2007). The pathological processes of chronic pain result in persistent noxious inputs and the influence of environmental factors may serve to maintain these inputs (Siddall & Cousins, 2004). The factors that predict chronicity of pain link to musculoskeletal conditions, the lifestyle of the individual and psychosocial factors (Bergman, 2007). Once pain is established it is

likely to persist in older individuals and those with other somatic symptoms (Papageorgiou, Silman, & Macfarlane, 2002).

In accordance with the theories of pain, one key biological factor for chronicity may be an underlying genetic vulnerability (Holliday & McBeth, 2011). Twin studies can help to establish the heritability of conditions through a better understanding of genetic and environmental influences. In 2004, Kato and colleagues studied 4,170 monozygotic, 5,881 same-sex dizygotic and 5,755 opposite-sex dizygotic twins aged 42 and over in Sweden and found differences in susceptibility to chronic widespread pain reflecting modest genetic and negligible family environment influences (Kato, Sullivan, Evengård, & Pedersen, 2006). The role of underlying genetic vulnerability for chronicity was also highlighted in a systematic review of twin studies of pain; Nielsen and colleagues (2012) reported heritability (the estimated proportion of observed variation in pain phenotype attributable to genetic influences) of 45-50% for migraine, tension-type headache and chronic widespread pain and 35% for back pain in adult samples (Nielsen, Knudsen, & Steingrímsdóttir, 2012).

In addition to genetic vulnerability, there are a number of lifestyle, health, social and psychological factors which reportedly predict pain chronicity. Examples include smoking, high BMI and poor diet (in women) (Vandenkerkhof, Macdonald, Jones, Power, & Macfarlane, 2011), female sex and lower socioeconomic status (Bergman, 2005; Davies et al., 2009; Fillingim, King, Ribeiro-Dasilva, Rahim-Williams, & Riley, 2009; Fuentes, Hart-Johnson, & Green, 2007; Macfarlane, Norrie, Atherton, Power, & Jones, 2009), physical trauma, occupational characteristics and traumatic life events (Holliday & McBeth, 2011). Social networks and social support have also been identified as important factors

influencing the persistence of chronic pain (Bergman, 2005). Patient beliefs regarding the meaning of symptoms, the ability to control their pain, impact on life and worry about the future have an important role in the persistence of chronic pain as a result of their effect on physical and psychological functioning, coping efforts, behavioural responses and response to treatment (Turk & Okifuji, 2002).

1.4.2 Location

Pain phenotypes can also be defined by specific anatomical site (regional pain), number of pain sites (multi-site pain) or a combination of anatomical area and number of painful sites (widespread pain).

Regional pain

Regional pain refers to pain occurring in an individual anatomical site such as the foot or lower back (Bergman, 2007; Jordan et al., 2010; Macfarlane et al., 2009). Comparisons between prevalence estimates are difficult due to the use of different definitions of the pain phenotype and of the method of estimating prevalence (e.g. point prevalence, lifetime prevalence) (see section 1.5.1). However, although prevalence estimates for regional pains differ due to variation in definition, most indicate that regional pain is common. A recent review reported the ranges for one month period prevalence in adults (18 and over) for neck pain was 15.4% to 45.3%, for low back pain was 24.0% to 49.5%, for shoulder pain was 18.6% to 31.0% and for knee pain was 13.0% to 28.0%. The pooled prevalence for foot pain was 28% (Table 1.1) (Henschke, Kamper, & Maher, 2015). Back pain is the most common regional pain; in the United Kingdom (UK), the range for point prevalence is 12% to 35% and for lifetime prevalence is 49% to 80% (Maniadakis & Gray, 2000).

Table 1.1 Prevalence figures for common regional pain sites in adults (reproduced from Henschke et al., 2015)			
Reference	**Number of included studies**	**Pain site**	**1 month prevalence (%)**
Hogg-Johnson et al., 2008	101	Neck pain	15.4-45.3
Hoy et al., 2010	5	Low back pain	24.0-49.5
Luime et al., 2004	19	Shoulder pain	18.6-31.0
Peat et al., 2001	5	Knee pain*	13.0-28.0
Thomas et al., 2011	31	Foot pain	28.0 (pooled prevalence)
*In adults 55 years and over			

Pain in one regional site has been shown to increase the likelihood of developing pain in other locations (Papageorgiou et al., 1996; Smith, Elliott, Hannaford, Chambers, & Smith, 2004). People often consult their GP for a single regional pain, most commonly in the back or knee, however most people will also be experiencing pain in other anatomical areas (Jordan et al., 2010).

Multisite pain

Multisite pain is defined as pain in two or more anatomical sites (Carnes et al., 2007; Lacey et al., 2014). Multisite pain is associated with greater functional problems than single site pain. There are strong linear relationships between an increasing number of pain sites and reduced general health, sleep quality, psychological health and functional ability (Kamaleri, Natvig, Ihlebaek, & Bruusgaard, 2008). In contrast to chronic widespread pain (CWP) (defined in the next section) multisite pain refers only to the number of pain sites and not to duration or location. The findings from a study of 2445 patients (aged 18-102 years) from 16 general practices (GP) practices in South East England demonstrated the difference in the prevalence of these phenotypes; 45% (n=1092) of the study population experienced chronic pain defined as pain for more than half of the days in the

previous year. Of the 1092 participants with chronic pain, 73% had pain in multiple body sites (two or more) but only 33% (n=285) of those with multi-site pain met the criteria for chronic widespread pain (Carnes et al., 2007).

Chronic widespread pain (CWP)

In 1990, Wolfe and colleagues developed the American College of Rheumatology (ACR) criteria for CWP and fibromyalgia. The aim of the criteria was to identify people with pain at the high end of the pain spectrum according to the extent, location and chronicity of their pain (Wolfe & Smythe, 1990); those with CWP have more pain resulting in higher impact than multisite and regional pain. Using these criteria individuals were identified as having widespread pain when they experienced pain in the axial skeleton, on the right and left sides of the body and above and below the waist. Individuals were identified as having fibromyalgia when they experienced widespread pain that is chronic (i.e. has lasted for at least three months (CWP) and tenderness in eleven of eighteen designated tender point sites (Wolfe & Smythe, 1990). These criteria have become the most widely used in epidemiological studies (McBeth & Mulvey, 2012). Prevalence figures for chronic widespread pain in studies using these criteria range from 4.2% to 13.2% (Gran, 2003). The prevalence of fibromyalgia in the general population has been estimated to range from 1 to 11% (McBeth & Mulvey, 2012).

Macfarlane and colleagues (1996) proposed the Manchester criteria for chronic widespread pain as an alternative to the ACR criteria (Macfarlane, Croft, Schollum, & Silman, 1996). They argued the ACR criteria were overly inclusive resulting in the misclassification of individuals to widespread pain when their pain was not sufficient to warrant inclusion. Macfarlane and colleagues proposed more stringent criteria which

demonstrated stronger associations with other symptoms such as fatigue, psychological distress and sleep problems (Hunt, Silman, Benjamin, McBeth, & Macfarlane, 1999). The Manchester definition of chronic widespread pain (CWP-M) defines chronic pain as pain that is present for at least three months in both the axial skeleton and at least two sections of two contralateral limbs. Macfarlane and colleagues (1996) suggested that the Manchester definition provided a more accurate representation of the concept of true widespread pain (Macfarlane et al., 1996). The point prevalence for chronic widespread pain using the Manchester definition was 4.7% (Hunt et al., 1999).

In response to a number of practical and philosophical limitations of the original ACR 1990 criteria including difficulties with the tender point count, the importance of fatigue, cognitive and somatic symptoms and variation of these amongst patients, a revised set of criteria was proposed in 2010 (Wolfe et al., 2010). Key revisions were that fibromyalgia be viewed as a continuous disorder rather than a dichotomous one (Wolfe & Michaud, 2009) and removal of the tender point count because in many cases, physicians were carrying out the tender point count inconsistently or not at all (Fitzcharles & Boulos, 2003). The true value of the tender point count was also questioned due to subjectivity, variable reliability and poor correlation with pain report (Fitzcharles & Yunus, 2012). The new criteria included a widespread pain index (WPI) and a symptom severity (SS) scale. The WPI measured the number of painful body regions ranging from 0-19 and the SS scale measured the severity and extent of fatigue, cognition, sleep and somatic symptoms on a scale ranging from 0-12. Patients were considered to meet the criteria for fibromyalgia if they scored 7 or above on the WPI and 5 or above on the SS scale, or between 3 and 6 on the WPI and 9 or above on the symptom severity scale (Wolfe et al., 2010). These

revisions to pain classifications demonstrate evolving attempts to accurately capture pain phenotypes and their impact. Despite criticisms, established criteria such as the ACR definition of CWP allow for some uniformity across studies of pain.

1.5 Epidemiology of pain

The epidemiology of pain provides information on the natural history and determinants of pain; this informs the view of pain as a public health problem, guides policy and informs methods to prevent and manage the condition from a clinical and population health perspective (Croft et al., 2010). Recognition of a condition as a public health problem is determined by the frequency and impact of that condition (Woolf et al., 2012). There is substantial literature on the prevalence and impact of pain phenotypes. The previous and following sections include a synthesis of recent reviews with the aim of providing a summary of current research of the extent of pain and its impact. A title and abstract search of PubMed was undertaken to identify articles published in the last five years using the search terms 'pain' and 'epidemiology' or 'burden', or 'impact' or 'consequences' and 'review' with the aim of capturing all recent general reviews of this topic. The review articles found are listed in Table 1.2. Reference lists of included reviews were also searched for key studies. The search was restricted to non-cancer pain in adults and did not include articles focussed on site specific pain or specific geographical locations (i.e. country-specific) as these were incorporated into broader reviews (Table 1.2). (Site-specific and country- specific information is presented in Table 1.1 and 1.3.)

Table 1.2 Results of PubMed search for reviews of the prevalence and impact of pain from 2010 to 2015		
Authors	**Year**	**Title**
Henschke N, Kamper SJ, Maher CG	2015	The epidemiology and economic consequences of pain
Molton IR, Terrill AL	2014	Overview of persistent pain in older adults
Moore R, Derry S, Taylor RS, Straube S, Phillips CJ	2014	The costs and consequences of adequately managed chronic non-cancer pain and chronic neuropathic pain
Breivik H, Eisenberg E, O'Brien T	2013	The individual and societal burden of chronic pain in Europe: the case for strategic prioritisation and action to improve knowledge and availability of appropriate care
Patel AS, Farquharson R, Carroll D, Moore A, Phillips CJ, Taylor RS, Barden J	2012	The impact and burden of chronic pain in the workplace
Phillips CJ, Harper C.	2011	The economics associated with persistent pain
Reid KJ, Harker J, Bala MM, Truyers C, Kellen E, Bekkering GE, Kleijnen J	2011	Epidemiology of chronic non-cancer pain in Europe: narrative review of prevalence, pain treatments and pain impact

1.5.1 Prevalence of pain

The prevalence figures of pain described in previous sections refer to the number of people who have existing pain at a particular point in time (point prevalence) or over a specified period of time (period prevalence). The prevalence of pain varies according to the definition of pain in terms of the length of time it is experienced for (e.g. acute, chronic), location, (e.g. site-specific, widespread) and also according to study population (e.g. working age (16-65), oldest old (85+) (Croft et al., 2010). Pain intensity is usually recorded using verbal rating scales, visual analogue scales or numerical rating scales (Croft et al., 2010) which results in heterogeneity between studies (Von Korff, Jensen, & Karoly, 2000).

Focusing on chronic pain, the World Health Organization Mental Health Surveys estimated the prevalence in adults in developed and developing countries to be 37.3% (95% confidence interval (CI) 36.7, 37.8%) and 41.1% (95%CI 40.3, 41.9%) respectively (Tsang et al., 2008). Participants were aged 18 and over in all surveys apart from those

from Japan (20 and over), Israel (21 and over) and New Zealand (16 and over). In these surveys, chronic pain was defined as “arthritis or rheumatism”, “chronic back or neck problems”, “frequent or severe headaches” or “other chronic pain”. This indicates potential misclassification, for example responders may have “arthritis” but not have chronic pain and the use of the term “arthritis” may vary between countries. Respondents were asked to indicate if their condition had been present in the 12 months prior to the survey (Tsang et al., 2008). In contrast, estimates from another international comparison study (15 European countries and Israel) indicated slightly lower prevalence estimates (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). In this large survey of chronic pain undertaken in 2003 (where chronic pain was defined as pain that lasts for more than six months and which increases to 5 out of 10 in intensity at least twice a week) in the general adult population (i.e. adults over 18 years) prevalence estimates ranged from 12% to 30% (Breivik et al., 2006).

A systematic review of the prevalence and impact of chronic non-cancer and neuropathic pain reported one in five adults experience at least moderate pain lasting three months or longer and one in fourteen adults experience chronic neuropathic pain (i.e. that pain occurs as a result of a lesion or disease of the somatosensory nervous system, (IASP, 2012)) (Moore, Derry, Taylor, Straube, & Phillips, 2014).

Despite the varying approaches to defining chronic pain, these studies indicate that it commonly occurs. Recognising how prevalence varies according to demographic characteristics (age, sex and socio-economic status) provides a starting point for identifying who are more likely to experience chronic pain.

1.5.2 The distribution of pain by age

The prevalence of chronic pain typically increases with age until the seventh decade (Thomas, Mottram, Peat, Wilkie, & Croft, 2007; Thomas, Peat, et al., 2004) when it then plateaus or decreases in the oldest age groups (Breivik et al., 2006; Helme & Gibson, 1999; Gran, 2003). The decrease in prevalence may be explained by older people not reporting pain because they see it as a normal part of ageing, a decrease in nociception with age and reduced activity levels leading to a reduction in stimulus for the experience of pain (Helme & Gibson, 1999). The underreporting of pain in older ages has been attributed to the presence of other medical problems, cognitive and sensory impairment and depression (Ferrell, 1991; Molton & Terrill, 2014). Notably despite the plateau of pain prevalence in older adults the impact of pain (i.e. pain that interferes with daily activities (work outside the home and housework)) continues to increase with age (Thomas, Peat, et al., 2004).

1.5.3 Distribution of the prevalence of pain by sex

Pain is more common in females than males for all pain definitions, with the exception of cancer pain) (Fillingim et al., 2009). For example, in adults aged 72 and over in the Framingham Heart Study, which is an observational cohort study of adults living in the community, 63% of women reported pain in one or more locations compared to 52% of men (Leveille, Zhang, McMullen, Kelly-Hayes, & Felson, 2005). The increased prevalence of pain in women occurs across age groups. One example of this is the prevalence of widespread pain in adults aged over 50 years in North Staffordshire (Thomas, Peat, et al., 2004). Women reported a higher prevalence of widespread pain in all age-stratified groups (i.e. 50-69, 60-69, 70-79, 80+ years) (Figure 1.4).

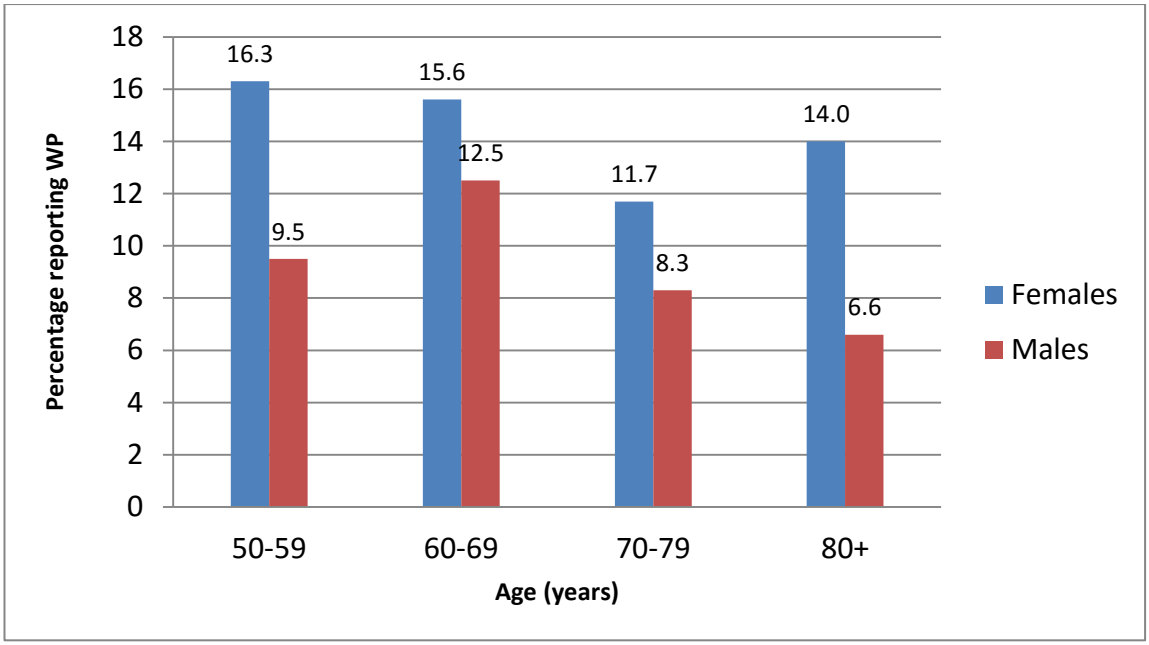


Figure 1.4 The prevalence of widespread pain (WP) in the North Staffordshire Osteoarthritis Project (NorStOP) stratified by age and sex n=7878. (Thomas et al., 2004)

The difference in prevalence between men and women may be due to biological (e.g. hormonal modulation) and psychosocial factors (e.g. women are more likely to catastrophise than men and men and women use different coping strategies) (Fillingim et al., 2009; Wijnhoven, de Vet, & Picavet, 2006). Irregular or prolonged menstrual cycle, hysterectomy, previous pregnancy, duration of oral contraception use and the use of estrogens during menopause are associated with low back pain and/or chronic upper extremity pain (Wijnhoven et al., 2006). Catastrophising is more common in women and this has been shown to explain sex differences in the report of pain (Fillingim et al., 2009). Pain coping strategies focussed on the sensory aspects of pain are more beneficial to men whereas females respond better to emotional focusing (Keogh & Herdenfeldt, 2002). Pain reporting may also be influenced by greater perceived social acceptance to complain about pain symptoms, greater exposures to risk factors for musculoskeletal pain (e.g.

psychosocial factors), or greater vulnerability to pain symptoms in women compared to men (Wijnhoven et al., 2006).

1.5.4 Distribution of pain by socio-economic status

Socioeconomic position refers to the position individuals or groups hold within the structure of society based on social and economic factors (Galobardes, Shaw, Lawlor, Lynch, & Davey Smith, 2006). Socioeconomic position can be measured at an individual or area level. Individual socio-economic status can be identified by occupation, level of education, employment status (unemployed yes/no, number of episodes of unemployment), income, housing status and access to a car (Galobardes et al., 2006). Area level indicators can be grouped into the domains of income, employment, health and disability, education, skills and training, crime, barriers to housing and services, and living environment; these can be combined to form a single overall Index of Multiple Deprivation (IMD) (Department for Communities and Local Government, 2010). Low socioeconomic position is associated with multiple definitions of pain. Macfarlane and colleagues demonstrated an association between low socioeconomic status and shoulder, forearm, low back, knee and chronic widespread pain (Macfarlane, Norrie, Atherton, Power, & Jones, 2009). Jordan et al., (2008) reported a higher incidence and prevalence of disabling pain in older adults living in more deprived areas according to IMD score which was only partially explained by individual risk factors such as perceived adequacy of income and low level of education (Jordan et al., 2008). There are a number of ways that socio-economic status can lead to the occurrence of pain. Manual occupation (the occupational indicator for low socio-economic status) is a proxy measure for physical and heavy jobs which are more likely to lead to pain (Coggon et al., 2013).

Low socioeconomic status is also associated with unhealthy lifestyle factors (i.e. poor diet and smoking), higher body mass index which also predict chronic widespread pain (Davies et al., 2009) and with higher rates of morbidity which are linked with increased prevalence of pain. (For example, low socioeconomic position is associated with depression (Everson, Maty, Lynch, & Kaplan, 2002) which is linked with increased levels of pain (Davies et al., 2009)).

1.5.5 Economic consequences of pain

The high prevalence of pain has a substantial impact on society, often described in terms of economic consequences. One way of judging the extent of economic consequences of a condition is to compare its costs to the Gross Domestic Product (GDP) of the country in which the estimate was calculated. The economic burden of pain is substantial, both in terms of direct healthcare costs and indirect costs through loss of economic productivity (e.g. lost workdays due to sickness or disability) (Patel et al., 2012; Phillips & Harper, 2011; Reid et al., 2011; Woolf et al., 2012). In the United States of America in 2010, the total cost of pain through healthcare costs and lost workdays was estimated to be between $560 and $635 billion (approximately 4% GDP) (Table 1.3). These figures are higher than for cancer ($243 billion), heart disease ($309 billion) and diabetes ($188 billion) (Gaskin & Richard, 2012). As previously stated, back pain is the most commonly experienced musculoskeletal pain in the UK (Woolf & Pfleger, 2003). The direct healthcare cost of back pain in the UK in 1998 was estimated to be £1,632 million with total costs coming to £12,300 million (approximately 5% GDP). The amount attributable to employment-related costs was approximately £10,668 million (Maniadakis & Gray, 2000). Costs are also high in other European countries. The societal costs of back pain in

Germany have been estimated to be €48.96 billion (2.2% of GDP) (Wenig, Schmidt, Kohlmann, & Schweikert, 2009) and the total indirect costs of chronic back and joint pain in Portugal has been estimated at €740 million (0.5% of GDP) (Breivik, Eisenberg, & O'Brien, 2013).

Table 1.3 displays the estimated total (direct plus indirect) annual costs of chronic pain for Australia, Denmark, Ireland, Sweden and the United States.

Table 1.3 Estimated total annual financial costs of chronic pain conditions for selected countries

Reference	Country	Year	National cost estimate/year	Approximate GBP equivalent*	Approximate Proportion of GDP
(The MBF Foundation, 2007)	Australia	2007	A$34.3 billion	17.7 billion	3%
(Christensen, Bilde, & Gustavsson, 2011)	Denmark	2010	DKK17.8 billion	1.8 billion	1%
(Raftery et al., 2012)	Ireland	2008	€5.34 billion	4.0 billion	3%
(Gustavsson et al., 2012)	Sweden	2008	€32 billion	24.1 billion	10%
(Gaskin & Richard, 2012)	United States	2010	$560-635 billion	372.3-422.2 billion	4%

*Exchange rates calculated using xe.com February 2015
GDP = Gross Domestic Product

The biggest contributor to the direct cost of pain is hospitalisation and the greatest contributor to the indirect costs are social benefits (e.g. disability allowance and unemployment benefits) (Breivik et al., 2013). Differences in definition, time and place of data collection and a lack of coding to classify chronic pain hinder the accurate estimation of the costs (Breivik et al., 2013; Moore et al., 2014; Patel et al., 2012). However, the figures outlined in Table 1.3 demonstrate the enormity of the economic burden of pain. Healthcare costs for patients with chronic pain are at least 2.6 times higher than for those without chronic pain irrespective of the location of the study and the types of healthcare costs included (Moore et al., 2014). The high economic costs of pain adds further to the need to reduce pain and its impact on individuals.

1.6 Impact of pain – a focus on mortality

The prevention of pain is often not possible and once established, is likely to persist, particularly in older adults (Papageorgiou et al., 2002). Understanding the nature and breadth of the consequences of pain is necessary to optimise its management; this will involve identifying targets for interventions to reduce its impact and subsequently improve the quality of life of those living with pain.

Whilst the relationship between pain and reduced physical and mental health and quality of life are more established, less is known about the natural course of pain. The long term health outcomes and links with mortality for people with pain are unclear (Macfarlane, McBeth, & Silman, 2001; McBeth et al., 2009). Pain may be a result of an underlying disease, or a marker for poor health which may lead to an increased risk of mortality (Andersson, 2009; Macfarlane et al., 2001; McBeth et al., 2009; Torrance , Elliot, Lee & Smith, 2010). Establishing if pain is associated with mortality and an understanding of how this occurs would highlight the need for and inform effective pain management. It may also highlight potential opportunities to reduce mortality risk by targeting specific impacts of pain. Despite its substantial and increasing impact on society, pain is not recognised as a public health problem in the same way as other health conditions such as cardiovascular disease and cancer (Woolf et al., 2012). Pain is a feature of many health conditions and its impact is obscured because it is the health condition which is the focus for research studies and clinicians (Blyth et al., 2015). If people with pain have an increased risk of mortality compared to those without pain, this would apply to a high number of people. This reinforces the need for a population level approach to the prevention of pain and indicates the need for better management of pain and its impact.

1.6.1 Studies of pain and mortality

All-cause mortality

There is no clear relationship between regional pain and all-cause mortality. Kåreholt and Brattberg (1998) reported increased rates of mortality across a 23 year period (1968 to 1991), in a representative sample of Swedish adults, for headache, chest pain, abdominal pain, pain in the extremities and rectal pain. However pain in the back, hips or shoulders was not associated with increased mortality during this period (Kåreholt & Brattberg, 1998). In contrast, using data from a representative sample of adults in the United Kingdom, Jordan and Croft (2010) reported significantly higher standardised mortality rates, for back, hip and shoulder pain after the first year of follow-up and for back pain the higher mortality risk remained over ten years of follow-up (Jordan & Croft, 2010).

Links between pain and mortality have been reported where the focus of the study has been on pain intensity or musculoskeletal conditions where pain is often the most common symptom. In a study where participants were asked to rate their pain on a scale from zero to ten with zero being 'no pain' and ten 'pain as bad as it could be', greater pain (above a score of 4 compared to equal or below 4) was associated with an increased risk of mortality over a 5 year follow up period (Sokka & Pincus, 2011). This study did not report the location or duration of pain. Increased mortality has also been reported in patients with osteoarthritis (Hochberg, 2008; Nuesch et al., 2011) and rheumatoid arthritis (Dadoun et al., 2013), although the role of pain is not clear. Although pain is the most common symptom of these diseases, they are not always markers for the presence of pain; for example, in osteoarthritis radiographic changes are not always present where

there are symptoms of joint pain and joint pain is not always reported when radiographic changes are present (Woolf et al., 2012). The impact of rheumatoid arthritis on mortality will have a number of pathways (e.g. via cardiovascular pathology (Dadoun et al., 2013)).

Cause specific mortality

An investigation of the relationship between pain and cause-specific mortality provides clues about potential mechanisms of a relationship between pain and mortality. Similar to all-cause mortality, overall there is no consensus for an association between pain and cause specific (cardiovascular disease, cancer) mortality.

For cardiovascular disease mortality, Zhu et al., 2007 reported an increased risk of mortality and coronary events for older women (aged 40 to 85 years) with daily back pain (Zhu, Devine, Dick, & Prince, 2007) and Penttinen et al., (1994) reported an association between back pain and an increased risk of death from ischaemic heart disease in men (Penttinen, 1994). Conversely Heliövaara and colleagues (1995) found no association between back pain and increased cardiovascular mortality in their study (Heliövaara, Mäkelä, & Aromaa, 1995).

For cancer mortality, McBeth et al., (2003) reported a link between pain and the incidence of cancer and reduced cancer survival, particularly breast and prostate cancers (McBeth, Silman, & Macfarlane, 2003). Jordan and Croft (2010) found an increased incidence of cancer diagnosis across all recorded regional pain sites but particularly for people with back pain (Jordan & Croft, 2010). In a study of confirmed fibromyalgia

patients and possible fibromyalgia patients (those referred for muscle pain and or tenderness but not meeting the criteria for fibromyalgia) Dreyer et al., (2007) found an increased risk of cancer in possible fibromyalgia patients but not in confirmed fibromyalgia patients (Dreyer et al., 2007). Cancer is associated with a number of lifestyle factors, for example the risk of breast cancer is linked with physical inactivity (Monninkhof et al., 2007). Physical inactivity is also associated musculoskeletal pain (McBeth & Nicholl, 2010) and this may be one mechanism by which those with pain have an increased mortality risk. In contrast however, Elliot et al., (2010) found no significant association between chronic pain and all cancers and no difference in cancer risk between those with severe or mild chronic pain (Elliott, Torrance, Smith, & Lee, 2010). Although the study undertaken by McBeth et al., (2003) reported an association between widespread pain and cancer mortality rather than chronic pain, 83% of the participants in this study met the IASP definition for chronic pain used by Elliot et al., (2010).

Overview of the studies of pain and mortality

Evidence for a relationship between pain and mortality is unclear. This is likely to be due to differences in the study populations and the different putative confounders included but particularly as a result of the different definitions of pain used. Chronic pain may be a useful starting point to examine the relationship between pain and mortality. There is potential for greater uniformity in case definition with use of recognised criteria (Merskey & Bogduk, 1994). As previously stated, chronic pain, that is pain that lasts for three months or longer (Merskey & Bogduk, 1994) is experienced by one in five adults (Moore et al., 2014) and commonly occurs in multiple body sites (Carnes et al., 2007). To evaluate

if there is a relationship between chronic pain and mortality, a systematic review was undertaken. In addition, the relationship between chronic widespread pain and mortality was examined in the review; chronic widespread pain, a sub-group of chronic pain and the cardinal symptom of fibromyalgia is linked with a greater impact than pain that is not widespread (Croft et al., 1996; Hunt et al., 1999; Kamaleri et al., 2008). Therefore if chronic pain is associated with mortality the relationship is likely to be strongest in those with chronic widespread pain. The systematic review of chronic pain and mortality is presented in Chapter Two.

1.7 Key messages

- Pain is a complex, subjective multifactorial experience that is common and has a substantial impact on individual health and the economy.
- It is unclear if pain is associated with an increased risk of mortality.
- The high prevalence of pain in the general population means that if there is a link with mortality the increased risk applies to a substantial number of people.

Chapter Two. Chronic pain and mortality: a systematic review and meta-analysis

2.1 Chapter summary

Chapter One introduced the prevalence, burden and impact of pain and the need to investigate whether people with pain have an increased risk of mortality. Evidence for a relationship between pain and mortality is inconsistent and may be due to the different definitions of pain applied. A comprehensive evaluation of existing studies on this topic would help to provide a clearer understanding of any relationship between pain and mortality. This chapter presents a systematic review of literature assessing the relationship between chronic pain and mortality; this involved evaluation and integration of existing evidence to determine if chronic pain was associated with an increased risk of mortality.

2.2 Introduction

Systematic reviews and meta-analyses are a fundamental part of health research, particularly in areas where conflicting findings arise in the literature (Egger, Smith, & Altman, 2001). They are undertaken to condense and integrate findings on a particular subject or a relationship in a strategic and comprehensive way (Mulrow, 1994). They can indicate a consensus, indicate the need for, or inform future studies. Systematic reviews provide evidence to aid the development of practice guidelines and government policy (Moher, Stewart, & Shekelle, 2012) and play an important role in preventing unnecessary

studies which may be expensive and time consuming yet will not contribute anything new to the field in question (Mulrow, 1994).

Systematic reviews of randomised control trials are useful for evaluating medical interventions, whereas systematic reviews of observational studies are used to assess aetiological hypotheses and assess the long term medical effectiveness of interventions (Egger et al., 2001). Systematic reviews do not provide discrete answers to specific questions; rather they bring together pieces of evidence to more completely assess and describe the topic of interest (Popay, Roberts, & Sowden, 2006).

2.2.1 Advantages and disadvantages of systematic reviews

The use of systematic reviews in healthcare is firmly established (Moher et al., 2012), and considered to be an invaluable scientific activity (Mulrow, 1994) however it is important to use some caution when using reviews to make decisions about healthcare. The advantages of systematic reviews are evident if the review is carried out comprehensively. These include providing an appraisal of literature in a systematic and reproducible way (Moher et al., 2012), summarising large amounts of data, identifying gaps in the literature, overcoming the limitations of individual studies by increasing power and precision and enabling generalisability of findings across different populations and settings to be established (Mulrow, 1994). They also help to overcome biases often seen in traditional narrative reviews (e.g. subjectivity, unreproducible) by ensuring a structured systematic approach, including appraisal of the quality and consistency of studies on a particular topic and providing an efficient way to evaluate specific topics (Egger et al., 2001). This helps to prevent unnecessary replication of existing work and improves the reliability and accuracy of recommendations (Petticrew, 2001).

Systematic reviews also have a number of disadvantages. They are time consuming and resource intensive (Egger et al., 2001). The inclusion of studies of poor methodological quality can compromise the overall findings by leading to poor or imprecise overall estimates, there may be a distortion of findings caused by publication bias (significant results are more likely to be published, and in English) and prior knowledge of studies can influence inclusion criteria when designing the review protocol (Egger et al., 2001). Statistical pooling (meta-analysis) is sometimes used inappropriately when it is not meaningful to do so (e.g. if the included studies are not directly comparable) and there can also be difficulties in identifying and including relevant unpublished literature (Petticrew, 2001).

In order to avoid the potential pitfalls involved in undertaking a systematic review it is important to have a clearly established protocol clarifying inclusion and exclusion criteria, quality assess all included studies using an established appraisal tool and ensure procedures are carried out by more than one reviewer (*Systematic reviews: CRD's guidance for undertaking reviews in health care*, 2009)**.** This systematic review followed an a priori determined protocol.

2.3 Aim

To determine the extent of association between chronic pain (and chronic widespread pain) and mortality.

2.4 Objectives

The objectives of this systematic review were:

1. To identify studies which have investigated the association between chronic pain and increased mortality.
2. To evaluate the quality of the evidence of an association between chronic pain and mortality.
3. To determine the strength and consistency of an association between chronic pain and mortality.

2.5 Methods

A protocol for the conduct of this systematic review and meta-analysis was developed with reference to Centre for Reviews and Dissemination (CRD) guidelines (*Systematic reviews: CRD's guidance for undertaking reviews in health care*, 2009) and consisted of four phases:

2.5.1 Phase 1: Search strategy and identification of studies (objective 1)

A comprehensive search strategy was conducted by a single observer (DS). Broad search terms were used to maximise the identification of all observational studies that have examined the link between mortality and chronic and/or widespread pain. The search strategy used subject headings (e.g. MeSH where possible) and text words for death (e.g. mortality, death, survival), pain (e.g. musculoskeletal pain, fibromyalgia, joint pain) and study type (e.g. cohort studies, longitudinal studies and cross-sectional studies) (see Appendix I for full search strategy). The following databases were searched in March 2012: Ageline, AMED, CINAHL, EMBASE, MEDLINE, PSYCHINFO, Social Sciences Citation Index (SSCI) and Science Citation Index Expanded (SCI-EXPANDED) using ISI Web of Science. The Cochrane databases (Cochrane Database of Systematic Reviews (Cochrane

Reviews) and the Database of Abstracts of Reviews of Effects (Other Reviews) (DARE) were searched for relevant reviews. Citation searches and reference list searches were undertaken to identify other possible relevant studies. A search of the Open Grey database for grey literature (www.opengrey.eu) was undertaken in April 2012 to identify any relevant papers. Searches in AMED, CINAHL, EMBASE, MEDLINE and PSYCHINFO were updated until March 2014.

2.5.2 Phase 2. Study selection (objective 1)

Identified studies were initially filtered with a title search by a single observer (DS) based on the following inclusion criteria:

- Study type - observational studies
- Participants – community dwelling adults
- Exposure – chronic (lasting more than 3 months) or widespread pain including fibromyalgia
- Outcome - mortality
- Papers published in English

Exclusion criteria

- **Study type** - trials
- **Exposure** - musculoskeletal conditions (e.g. osteoarthritis), specific locations of pain only (e.g. knee pain, back pain), studies focussed on non-musculoskeletal pain (e.g. cancer pain).
- **Outcome** – disease incidence.

The abstracts and keywords of the remaining studies were screened by two reviewers (DS) (RW) in order to minimise human error before the retrieval of full text studies for further screening. Any disagreements regarding inclusion were discussed in a consensus meeting with a third reviewer (JM) to finalise which papers would be included in the review.

2.5.3 Phase 3: Data extraction and quality assessment (objective 2)

From each included study, data on study population, follow-up period, pain phenotype, outcome, cause of death and potential confounding factors, were extracted by one reviewer (DS) and checked by two others (RW) (JM) for omissions and accuracy (Table 2.1). One of the most important aspects of conducting a systematic review is to assess the quality of the included studies. Quality can be defined as the extent to which a study attempts to minimise bias and error in its design, conduct and analysis (Khan, Kunz, Kleijnen, & Antes, 2003). If the included studies in a systematic review were of poor quality the overall findings are unlikely to be generalisable and could be potentially meaningless.

Sources of bias

Bias in research studies can produce results that are systematically different from the truth (Khan et al., 2003). Observational studies have a number of potential sources of bias. These include:

- **Selection bias**

  This occurs where the study population differs from, and therefore is not representative of, the target population (Grimes & Schulz, 2002). Participants in

observational studies are grouped according to their disease status or their exposure to a particular risk factor and selection bias can occur due to differential surveillance, diagnosis or referral to the study (Hennekens & Buring, 1987).

Non-response bias is one form of selection bias where the participants who don't respond in a study differ from those who do, for example where those who choose to take part are healthier than those that do not (i.e. the healthy volunteer effect) (Delgado-Rodríguez & Llorca, 2004). Non-response is often greater in males and older people and is influenced by level of education, socioeconomic status and the perceived benefits of taking part in the study (Silman & Macfarlane, 2002). In order to assess this form of bias information is needed about individuals who choose not to take part.

A similar form of bias in cohort studies can result from loss to follow up (attrition) which occurs when participants are followed over time and fewer participants respond at later time points than at baseline. Those lost differ from those who remain in the study, meaning that any observed association will be an overestimate or underestimate of the true effect (Hennekens & Buring, 1987).

- **Information bias**

  Information bias occurs when there is measurement error in the data, that is, the true value differs from that which is observed (Hennekens & Buring, 1987). It is also referred to as observation, classification or measurement bias (Grimes & Schulz, 2002). Forms of information bias include:

  - Recall bias - this occurs when there are differences in the likelihood of reporting an event based on context or emotional state. For example, individuals who are aware they have been subject to a particular exposure may be more likely to report disease symptoms than those not exposed (Delgado-Rodríguez & Llorca, 2004).
  - Reporting bias - this occurs when participants give answers they perceive are in the direction of interest; favourably report socially desirable behaviours such as physical activity or underreport socially undesirable behaviours such as alcohol consumption (Delgado-Rodríguez & Llorca, 2004).
  - Interviewer bias – this occurs when there are differences in the way that information is obtained, recorded or interpreted (Hennekens & Buring, 1987). For example, previous knowledge of a participant's exposure status may result in leading questioning in favour of an hypothesis of interest (Silman & Macfarlane, 2002).
  - Misclassification bias - this can occur where the procedure to measure the exposure or disease of interest is inaccurate resulting in the misclassification of participants as exposed or diseased when they are not (Delgado-Rodríguez & Llorca, 2004). Some degree of random

misclassification is likely to occur in most epidemiological studies, but becomes a problem if the proportion of misclassifications vary between the groups being studied (Hennekens & Buring, 1987).

- **Confounding**

  Confounding occurs when an attempt to measure the relationship between an exposure and outcome is actually measuring the effect of a third confounding variable (Grimes & Schulz, 2002). It can lead to an overestimation, underestimation, or change in direction of the true effect (Hennekens & Buring, 1987). A confounder is a variable that is associated with the exposure and outcome in question but is not on the causal pathway between the exposure and the effect (Delgado-Rodríguez & Llorca, 2004). For example, an increased incidence of lung cancer in coal miners working at the coal face compared to miners working at the surface could be explained by coal face workers smoking more than those who work at the surface. Smoking would be the confounding factor that explains the observed relationship between coal face working and lung cancer (Silman & Macfarlane, 2002).

Quality assessment tools

An important distinction needs to be made between the quality of the reporting of studies and the quality of the design, conduct and analysis of studies (Sanderson, Tatt, & Higgins, 2007). A number of checklists are available to guide the reporting of studies for example, the Strengthening of Reporting of Observational Studies (STROBE) (Von Elm et al., 2007), and Meta-analysis of Observational Studies in Epidemiology (MOOSE) (Stroup,

Berlin, & Morton, 2000). These guidelines are designed to help authors ensure comprehensive reporting of the study they have undertaken. Tools designed to assess susceptibility to bias are aimed at assessing the validity of the studies (Sanderson et al., 2007). These range from simple checklists (Kmet, Lee, & Cook, 2004) to rating scales such as the Newcastle-Ottawa scale (Wells et al., 2000). There is no consensus over which tool is the best for assessing the quality of observational studies. Sanderson and colleagues (2007) conducted a review of available quality assessment tools and identified 86 in total and recommended that quality assessment tools should; include a small number of key domains, be as specific as possible (with consideration of the study design and topic area), be a simple checklist rather than a scale and show evidence of validity and reliability (Sanderson et al., 2007).

Quality in Prognosis Studies tool

The Quality in Prognosis Studies tool (QUIPs) was chosen for this review as it provides a number of criteria for assessing the risk of selection bias, non-response bias, measurement bias and confounding and was developed through expert international consensus (Appendix II) (Hayden, Côtė & Bombardier, 2006). The following areas are assessed: study participation, study attrition, measurement of exposure, measurement of and controlling for confounding variables, measurement of outcomes, and analysis approaches. For this review, the QUIPs tool was modified slightly for use with cross sectional studies. The reviewers assessed for non-response bias in place of attrition and the prognostic factor measurement component was used to apply to any factor (exposures and outcomes). For each of the potential areas for bias, reviewers assessed whether the study methods satisfied between three and seven general statements (e.g.

"the source population or population of interest is adequately described for key characteristics") and one overall statement (e.g. "Is the following statement satisfied based on responses to the above questions; the study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results?"). Reviewers rated their agreement as "Yes", "Partly", "No", "Unclear", or "Not Relevant". The assessment of the methodological quality of each of the selected studies was carried out independently by two reviewers (DS, RW). A third reviewer (JJ) was asked to review selected studies to ensure consistency and enable a consensus to be reached over any disagreements. Where reviewers agreed 'yes' to the overall statements the risk of bias was low, 'partly' or 'unclear' the risk was moderate and 'no' indicated high risk of bias in that area.

Inter-rater agreement

The level of agreement between the two reviewers when assessing potential bias in the identified studies was examined using percentage agreement. While this illustrates the amount of agreement between reviewers, it does not account for the agreement that may be expected by chance (Sim & Wright, 2005). The Kappa statistic calculation is based on the difference between the observed agreement (percentage figures) and the level of agreement that would be expected by chance alone (Fleiss, 1971). The measure is standardised to lie on a scale between -1 and 1 where 1 indicates perfect agreement, 0 indicates what would be expected by chance and negative values indicate agreement worse than would be expected by chance (Viera & Garrett, 2005). An interrater reliability analysis using the Kappa statistic was therefore undertaken on the overall scores to determine the level of agreement among reviewers. The Kappa statistic can be calculated

using weighted or unweighted methods. Weighted methods assign greater importance to more serious disagreements in ordinal scales (Sim & Wright, 2005). For example, a greater weight would be assigned to the difference between 'neither agree nor disagree' and 'strongly agree' than the difference between 'agree' and 'strongly agree' in a rating scale. This analysis used an unweighted calculation performed in SPSS version 20. Although it is more appropriate to use a weighted Kappa for ordinal scales (Sim & Wright, 2005) an unweighted version was deemed more appropriate for this rating scale because one of the response options was 'not relevant' which is not equivalent to a one or more scale point difference than any of the other options. It was therefore considered more appropriate to use unweighted Kappa and treat all disagreements equally. Kappa values of ≤0 indicate poor agreement, 0.01–0.20 slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, and 0.81–1.00 indicates almost perfect agreement (Landis & Koch, 1977).

2.5.4 Phase 4: Data extraction and analysis (objective 3)

Meta-analyses are not always a part of systematic reviews but can provide useful additional information if used appropriately. Meta analyses of observational studies are often challenging due to the inherent problems of bias and confounding often seen in observational studies, however, they can also be used to help understand and quantify sources of variability across studies (Stroup et al., 2000).

Where a meta-analysis is included as part of a systematic review it can be used to statistically combine the findings of a group of studies in order to produce a weighted average effect (Khan et al., 2003). The overall pooled effect is calculated and presented with the accompanying statistical test of significance (z test and associated p- value)

(Gliner, Morgan, & Harmon, 2003). Meta-analyses also provide a statistical test of heterogeneity to determine whether the studies are consistent (Higgins, Thompson, Deeks, & Altman, 2003). Heterogeneity is defined as the presence of variation in true effect sizes across studies (Higgins, 2008) and is quantified using the I^2 statistic. The I^2 value lies between 0 and 100% and represents the percentage of the total variation across studies that is due to heterogeneity rather than chance (Higgins et al., 2003). Higgins and colleagues (2003) suggest I^2 values of 25% can be considered low, 50% moderate and 75% high (Higgins et al., 2003).

A chi-squared test of goodness of fit and corresponding p-value are also calculated in meta-analyses to determine whether the amount of heterogeneity (I^2 value) is significant (Gliner et al., 2003). This test assesses whether observed differences in results are the result of chance alone. A low p value (or a large chi-squared statistic relative to its degree of freedom) indicates variation in the effect estimates beyond what would be expected by chance (Higgins, Green, & Collaboration, 2008). Finally, the Tau-squared value is also calculated which is a point estimate of the between study variance. The I^2 value is therefore a measure of the proportion of variability due to Tau squared rather than within-study error (Higgins, 2008).

A meta-analysis was therefore conducted to quantify heterogeneity and where possible determine a pooled effect for the relationship between chronic pain and mortality. Meta-analyses can be undertaken using either a fixed or a random effects statistical model (Riley, Higgins, & Deeks, 2011). A fixed effects model assumes all of the included studies are measuring the same effect and any differences are due to chance whereas a random effects model allows for differences in the effect between the studies (Riley et al., 2011).

As the ten studies included in the review included different study populations, different measures of potential confounders and different definitions of the exposure it was assumed there would be a high degree of heterogeneity between studies, therefore a random effects model was used.

The logarithm of the measure of effect (Mortality Rate Ratio) and accompanying confidence intervals were calculated in order to perform the analysis. This transformation was used to reduce skewness in the data. For ratio summary statistics the scale is not symmetric as the lowest number which it can take is zero and the highest infinity. The log transformation makes the scale symmetric and suitable for analysis (Deeks, Higgins & Altman, 2008).

Variation in the definition of chronic pain (pain phenotype) was expected to be a key source of heterogeneity and was therefore explored in a sensitivity analysis, only including studies using the stricter definition of widespread pain. The pooled effects, chi-squared tests, corresponding p-values, I^2 values and Tau-squared values were calculated (described above) combining studies measuring:

i) Chronic pain and all-cause mortality

ii) Chronic widespread pain and all-cause mortality

iii) Chronic pain and cancer mortality

iv) Chronic widespread pain and cancer mortality

v) Chronic pain and cardiovascular disease mortality

vi) Chronic widespread pain and cardiovascular disease mortality

vii) Chronic pain and respiratory disease mortality

viii) Chronic widespread pain and respiratory disease mortality

All statistical analysis was performed in Stata 12 where the random effects model implemented was that of DerSimonian and Laird (1986) (DerSimonian & Laird, 1986).

Narrative review

A narrative review was undertaken to explore differences and similarities between included studies for age and sex, follow-up time, pain phenotype, population characteristics, methods of analysis and potential confounding factors included. Sources of heterogeneity are presented and linked to the study findings descriptively and in tabular form (Table 2.3).

Crude results were not available for all studies so the meta-analysis used the maximally adjusted results for each study. Two of the studies used standardised mortality ratios (SMRs) as their measures of effect (Dreyer, Kendall, Danneskiold-Samsøe, Bartels, & Bliddal, 2010; Wolfe, Hassett, Walitt, & Michaud, 2011) and one used adjusted odds ratios (AORs) (Smith, Elliott, & Hannaford, 2003). These are not directly comparable to mortality rate ratios (MRRs) therefore results from these studies were not included in the calculation of pooled estimates.

2.6 Results

2.6.1 Identification of studies

The search identified 15,057 articles. 15,006 were excluded during the review of titles as they did not meet the inclusion criteria (Figure 2.1). The review of abstracts and keywords resulted in the exclusion of a further 30 articles. The full texts of 21 articles were retrieved for further screening and 9 of these were excluded; for 6 of these studies it was

not possible to determine the presence of widespread pain or chronic pain lasting beyond three months (Ahmad & Bath, 2005; Elliott, Hannaford, Smith, Wyke, & Hunt, 2006; Jordan & Croft, 2010; Kåreholt & Brattberg, 1998; Khang & Kim, 2010; Sha et al., 2005), one study was focussed on inpatients in a pain management clinic (Maruta, Malinchoc, Offord, & Colligan, 1998), one study focussed on disease incidence as the outcome (Dreyer et al., 2007) and one examined the relationship between lifestyle factors and chronic widespread pain (Vandenkerkhof et al., 2011). Twelve articles describing nine studies remained; three articles were excluded to avoid using results from the same cohort multiple times in the analysis (Andersson, 2004; Mäkelä & Heliövaara, 1991; McBeth et al., 2003) leaving nine studies for the analysis. An additional study was added from the automated database search updates in 2013 (Nitter & Forseth, 2013) resulting in 10 studies in total. There was wide variation between the identified studies in terms of pain phenotype, follow-up time, population characteristics and inclusion of confounders (Table 2.1).

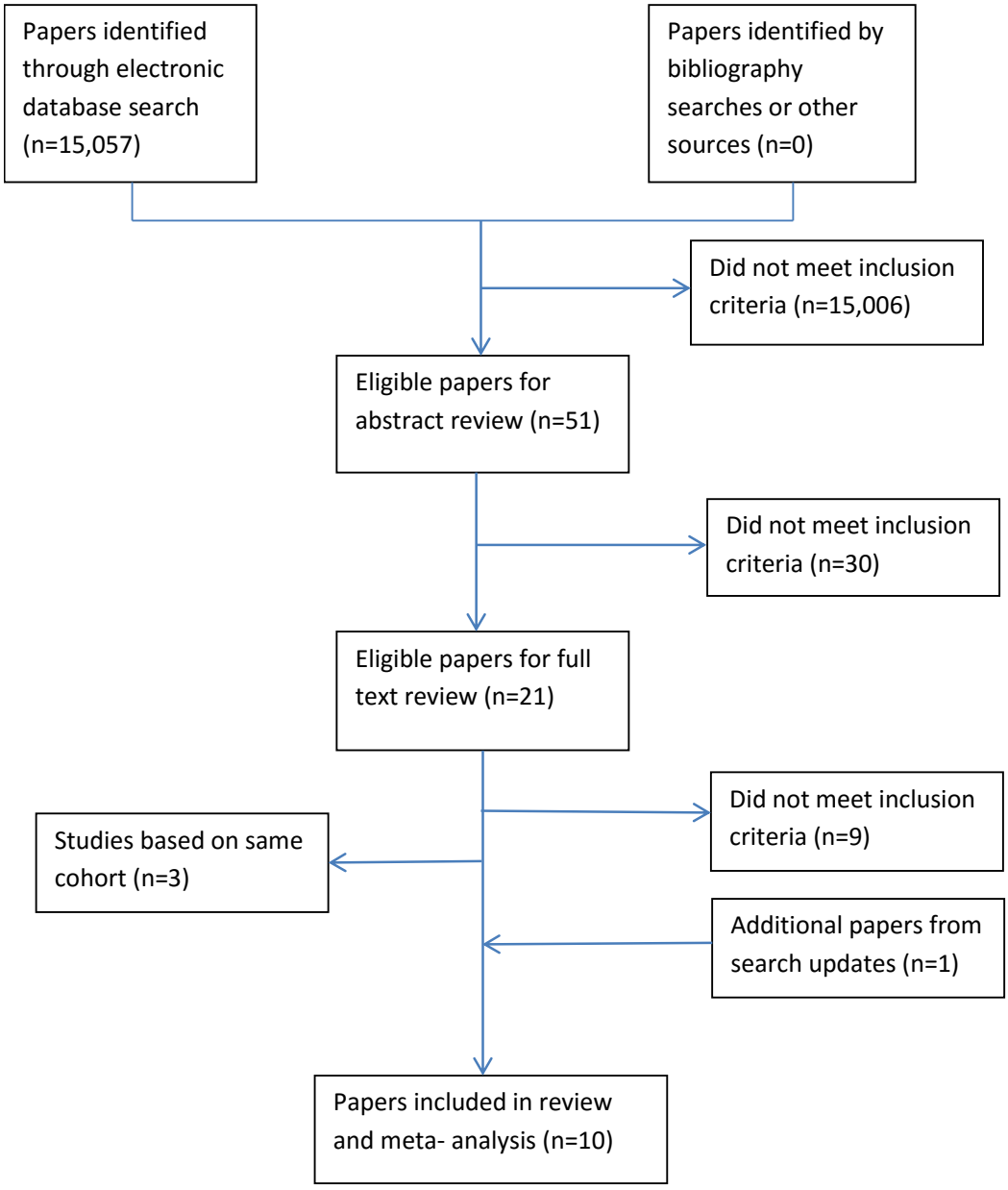


Figure 2.1 Flow chart of the selection of papers for the systematic review

Table 2.1 Summary of the papers included in the systematic review									
Study	**n**	**Age**	**% female**	**Location**	**Follow-up**	**Pain phenotype**	**All-cause mortality**	**Cause specific mortality (adjusted results)**	**Putative confounders**
Macfarlane, G.J. et al. (2001)	6569	18-85	58	North West England	8yrs	Widespread pain ACR (1990) criteria	MRR (95%CI) 1.31 (1.05-1.65)	MRR (95%CI) Cancer 2.07 (1.37 - 3.13) Cancer without prior diagnosis 2.27 (1.46-3.54) Cardiovascular disease 1.12 (0.78-1.61) Respiratory disease 1.01 (0.57-1.79) Other diseases 0.91 (0.45-1.85) All external causes 5.21 (0.94-28.78)	age, sex, study location
Macfarlane, G.J. et al. (2007)	7182	30 and over	54	Finland	14-16yrs	Widespread pain - in at least 4 sites (face validity with ACR (1990) criteria)	MRR (95%CI) 0.86 (0.74-1.00)	MRR (95%CI) Cardiovascular disease 0.83 (0.68-1.02) Cancer 0.64 (0.46-0.91) Respiratory diseases 0.89 (0.54-1.49) Other disease related 1.39 (0.88-2.19) Non disease related 1.39 (0.75-2.58)	age, gender, education, physical work stress, mental work stress, alcohol consumption, tobacco smoking, BMI
Andersson, H.I. (2009)	1609	25-74	50	Sweden	14 yrs	Widespread pain - in more than four pain locations including upper and lower body and axial pain (to get close to ACR criteria)	MRR (95%CI) Crude 1.95 (1.26-3.03) Adjusted 1.09 (0.62-1.90)	MRR (95%CI) Cardiovascular disease 2.17 (1.12-4.21) Cancer 1.15 (0.52-2.55) Other 1.18 (0.47-2.99)	Age, sex, living alone, contact with friends, club membership, chronic disease, smoking, physical activity, perception of stress, BMI, insomnia (cause specific results adjusted for age and sex)
McBeth, J. et al. (2009)	4515	16 and over	51.6	North West England	8.2yrs	Widespread pain ACR (1990) criteria. Number of pain sites	MRR (95%CI) Crude 2.4 (1.9-2.9) Adjusted 1.3 (1.1-1.5)	MRR (95%CI) Cancer 1.8 (1.3-2.6) Cardiovascular disease 1.3 (0.99-1.6) Respiratory disease 1.0 (0.7-1.6) All external causes 0.6 (0.1-3.8) Other 0.8 (0.5-1.4)	age, sex, practice, ethic group, Townsend score of deprivation

Sjøgren P. et al. (2010)	2242	16 and over	51.3	Denmark	8 years	Chronic pain (6 months or more)	MRR (95%CI) Adjusted 1.21 (1.02-1.44)		age, sex, education, marital status, BMI, smoking, antidepressant use, anxiolytic use, self-reported circulatory diseases, infectious or parasitic diseases, diabetes and mental disorders
Torrance N. et al. (2010)	5853	Mean 58.43	52.7	North East Scotland	10 years	Chronic pain (more than 3 months)	MRR (99%CI) Crude 1.32 (1.14-1.54) Adjusted 0.90 (0.74-1.07)	MRR (99% CI) All circulatory system 0.86 (0.65-1.14) Acute MI 1.11 (0.67-1.83) Ischaemic heart disease 1.04 (0.51-2.12) Cerebrovascular disease 0.58 (0.35-0.97) Other circulatory system 0.88 (0.47-1.66) All neoplasms 0.91 (0.64-1.28) Digestive organ neoplasms 0.97 (0.50-1.87) Respiratory organ neoplasms 0.81 (0.43-1.54) Other malignant neoplasms 0.95 (0.58-1.59) All respiratory diseases 1.23 (0.67-2.25) Pneumonia 1.44 (0.57-3.61) Chronic lower respiratory disease 1.35 (0.49-3.73) Other respiratory disease 1.08 (0.29-4.04) Diseases of the digestive system 0.90 (0.35-2.34) Diseases of the nervous system 0.42 (0.14-1.26) Other 0.96 (0.57-1.62)	age, sex, education, housing, long term limiting illness

Nitter A.K. & Forseth K.Ø. (2013)	2038	20 -68 years	100	Arendal, Norway	18 years	Chronic widespread pain (in muscles and joints and back or whole body for 3 months or longer)	MRR (95%CI) 2.8 (1.3-6.1)		age, sleep problems, feeling anxious, frightened or nervous, number of non-specific health complaints
Dreyer, L. et al. (2010)	1353	19 and over	94	Denmark	15 yrs (Mean 3.9 years)	ACR (1990) definition of FM	SMR (95%CI) 1.25 (0.9-1.7)	SMR (95%CI) Female only: Ischemic heart disease 0.3 (0.0-1.6). Other heart disease 3.0 (0.6-8.9) Cerebrovascular disease 3.1 (1.1-6.8) Cancer 0.6 (0.3-1.2) Pneumonia 2.7 (0.0-14.8), COPD 2.0 (0.5-5.2) Liver cirrhosis 6.4 (2.3-13.9) Mental disorders 2.3 (0.0-12.6) Suicide 10.5 (4.5-20.7) Other external causes 3.9 (0.1-21.7) Other 0.4 (0.1-1.5)	Standardised to Danish population (according to age, sex, calendar month)

Wolfe, F. et al. (2011)	8186	Mean 50.5, (SD 12.4)	94	USA	35yrs (Mean 7.3 years)	Fibromyalgianess scale. Widespread pain index. ACR definition of FM 1990, 2010.	SMR (95%CI) 0.90 (0.61-1.26)	SMR (95%CI) Heart diseases 0.84 (0.68-1.04) Cancer 0.95 (0.76-1.18) Accidents 1.45 (1.02-2.06) Chronic lower respiratory diseases 1.09 (0.74-1.62) Influenza and pneumonia 1.69 (1.12-2.57) Septicaemia 2.49 (1.61-3.68) Suicide 3.31 (2.15-5.11) Cerebrovascular diseases 0.75 (0.48-1.17) Nephritis/nephrotic syndrome/nephrosis 0.93 (0.50-1.72) Alzheimer's disease 0.57 (0.29-1.13) Essential hypertension/hypertensive renal disease 0.95 (0.40-2.23) Chronic liver disease and cirrhosis 0.47 (0.16-1.38) Parkinson's disease 0.22 (0.00-1.23) Assault (homicide) 0.26 (0.00-1.51)	Standardised to U.S. population (according to age, sex, calendar month)
Smith, B.H. et al. (2003)	10073	42-81 years	100	UK wide	6 years	Chronic pain (more than 3 months)	AOR (95%CI) 1.1 (0.81-1.26)	AOR (95%CI) All cancers 0.85 (0.62-1.18) Cardiovascular disease 0.95 (0.63-1.44) Respiratory disease 2.22 (1.12-4.39) Other diseases 1.08 (0.52-2.27) All external causes 0.99 (0.16-5.93)	age, social class, smoking

ACR = American College of Rheumatology
MRR = Mortality Rate Ratio
SMR = Standardised Mortality Ratio
AOR = Adjusted Odds Ratio
CI = Confidence Interval

2.6.2 Quality assessment

Table 2.2 presents the agreed level of bias for each area for each study. Across the studies there were two areas where reviewers agreed the risk of bias was most likely. The first was 'non-response'; this was due to the lack of information available about participants who did not respond to requests to take part in the studies. The second was 'confounding measurement and account'; there are a large number of potential confounders that may influence the association between chronic pain and mortality and these were accounted for in varying degrees in each of the studies. Where a small number of potential confounders were included in the analysis the reviewers considered the risk of bias to be high. Despite there being two areas where bias was likely, overall, all papers were deemed to be of adequate quality for inclusion in the review.

The level of agreement between the reviewers for all studies was substantial or almost perfect (Kappa statistic range 0.66 (95%CI 0.47, 0.86) to 0.96 (95%CI 0.88-1.04) (Table 2.2).

Table 2.2 Summary of agreed level of bias between the two reviewers and percentage agreement for each potential area of bias and overall Kappa for each study

Study	Participation		Non-response		Factor Measurement		Outcome Measurement		Confounding Measurement and Account		Analysis		Overall	Overall Kappa (95% CI)
	% agreement	Agreed level of bias	% agreement	Agreed level of bias	% agreement	Agreed level of bias	% agreement	Agreed level of bias	% agreement	Agreed level of bias	% agreement	Agreed level of bias	% agreement	
Macfarlane, G.J., et al. (2001)	67%	Moderate	100%	Moderate	100%	Low	100%	Low	88%	High	80%	Low	89%	0.85* (0.70, 0.99)
Smith B.H. et al., (2003)	100%	Moderate	100%	Moderate	100%	Low	100%	Low	88%	Moderate	80%	High	94%	0.86* (0.73, 0.99)
Macfarlane, G.J. et al. (2007)	83%	Low	67%	Moderate	100%	Low	100%	Low	88%	Moderate	60%	Moderate	83%	0.73* (0.54, 0.92)
Andersson, H.I. (2009)	67%	Moderate	83%	Moderate	100%	Low	100%	Low	100%	Low	100%	Low	95%	0.85* (0.70, 1.00)
McBeth, J., et al. (2009)	100%	Low	50%	Moderate	100%	Low	100%	Low	100%	Moderate	80%	Low	89%	0.79* (0.62, 0.97)
Dreyer, L., et al. (2010)	83%	Low	67%	Low	86%	Low	75%	Low	75%	High	80%	Moderate	78%	0.66* (0.47, 0.86)
Sjogren, P. et al. (2010)	83%	Moderate	67%	Moderate	100%	Moderate	100%	Low	63%	Low	100%	Low	83%	0.69* (0.48, 0.89)
Torrance, N. et al. (2010)	100%	Moderate	83%	Moderate	100%	Low	100%	Low	100%	Low	100%	Low	97%	0.96* (0.88, 1.04)
Wolfe, F., et al. (2011)	100%	Low	100%	Low	100%	Low	100%	Moderate	88%	Moderate	80%	Low	92%	0.88* (0.74, 1.00)
Nitter, A.K. et al. (2013)	100%	Moderate	100%	Moderate	86%	Moderate	75%	Moderate	75%	Moderate	60%	Moderate	83%	0.80* (0.64, 0.97)

* $p<0.05$

2.6.3 Study findings

In crude analyses one study reported that chronic pain was associated with mortality: MRR 1.32; 95%CI 1.14, 1.54 (Torrance et al., 2010), and two studies reported that widespread pain was associated with all-cause mortality: MRR 2.4; 95%CI 1.9, 2.9 (McBeth et al., 2009) and MRR 1.95; 95%CI 1.26, 3.03 (Andersson, 2009). In the first of these studies the association between chronic pain and mortality was no longer significant following adjustment for age and sex, education and housing (MRR 1.15; 95%CI 0.97, 1.35 (Torrance et al., 2010). In the second of these studies the association remained significant following adjustment for age, sex, medical practice, ethnic group and Townsend score of deprivation (MRR 1.3; 95%CI 1.1, 1.5) (McBeth et al., 2009). In the third study, the association remained significant after adjustment for age and sex (MRR 1.54; 95%CI 1.01, 2.35) but was not significant following adjustment for living alone, contact with friends, club membership, comorbidity, smoking, physical activity, BMI, perception of stress and insomnia (MRR 1.09; 95%CI 0.62, 1.90) (Andersson, 2009). Macfarlane and colleagues (2001) did not report crude results but did report a significant association between widespread pain and all cause-mortality following adjustment for age, sex and study location (MRR 1.31; 95%CI 1.05, 1.65) (Macfarlane, McBeth, & Silman, 2001). In adjusted analyses Sjøgren and Grønbæk (2010) reported a significant association between chronic pain and mortality (MRR 1.21; 95%CI 1.02, 1.44) (adjusted for age, sex, education, marital status, BMI, smoking, use of antidepressants, use of anxiolytics, self-reported circulatory diseases, diabetes and mental disorders) (Sjøgren & Grønbæk, 2010) and Nitter and Forseth (2013) reported an association between chronic widespread pain and mortality (MRR 2.80; 95%CI 1.3, 6.1) (adjusted for age, sleep problems, feeling

anxious, frightened or nervous, number of non-specific health complaints) . Dreyer et al (2010) reported borderline significantly increased mortality in participants with fibromyalgia (SMR 1.25; 95%CI 0.90, 1.70) (Dreyer et al., 2010). The remaining three studies did not report significant or strong associations between chronic or widespread pain and all-cause mortality (Macfarlane et al., 2007; Smith et al., 2003; Wolfe, Hassett, et al., 2011) (Table 2.1).

2.6.4 Evidence synthesis: meta-analysis

All-cause mortality

The results of the seven (of ten) studies which calculated mortality rate ratios (MRR) were combined to give pooled estimates. For the association between chronic pain and all-cause mortality, the analysis showed high statistical heterogeneity (I^2 = 78.8%), with MRRs ranging from 0.86 to 2.80. The pooled estimate was modest but not significant: MRR 1.14; 95%CI 0.95, 1.37 (p=0.162) (Figure 2.2). The sensitivity analysis including only studies measuring widespread pain indicated a slightly higher risk of mortality although the association was not significant and heterogeneity remained high (MRRs ranged from 0.86 to 2.8, I^2 = 82.3%, pooled MRR 1.22; 95%CI 0.93, 1.60 (p=0.157)) (Figure 2.3).

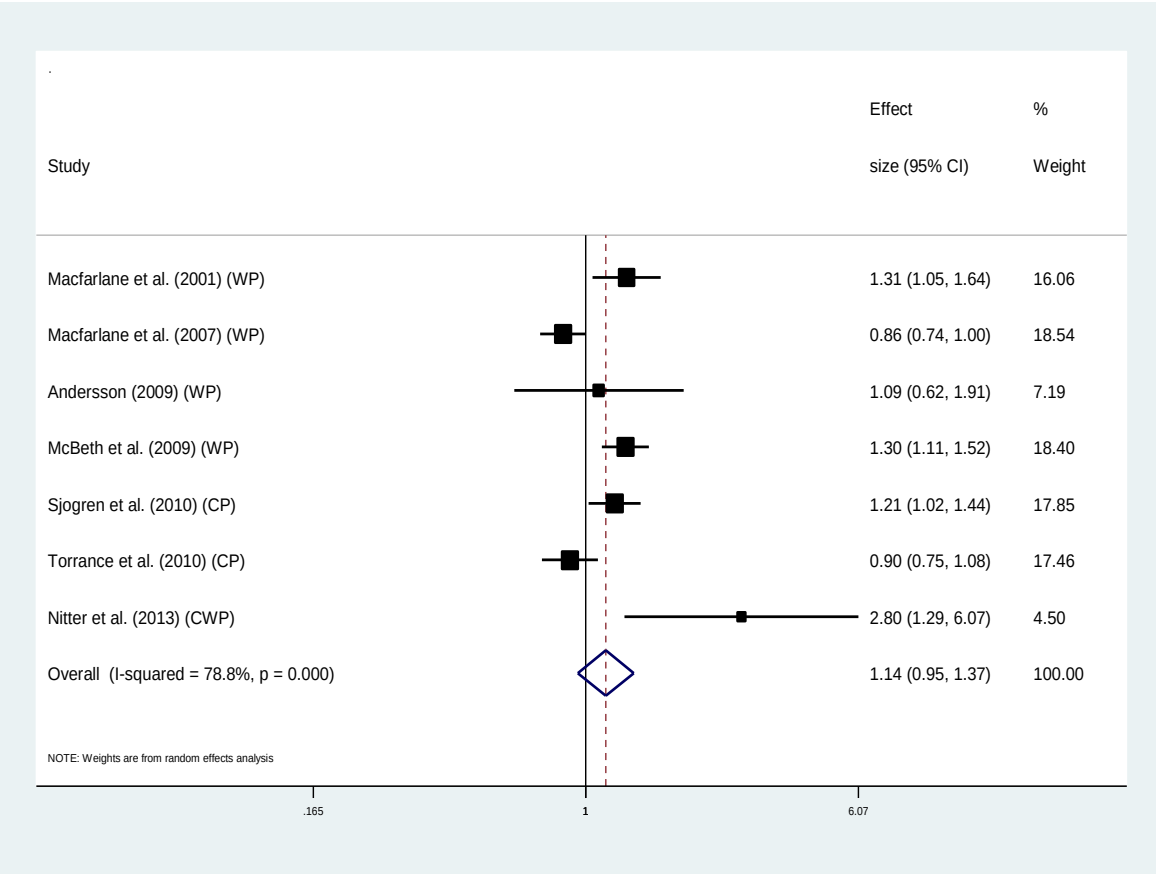


Figure 2.2 Forest plot of the of the association between chronic pain and all-cause mortality in identified studies (effect sizes are MRR only)

MRR=Mortality Rate Ratio, CI= Confidence Interval, WP = Widespread Pain, CP=Chronic Pain, CWP = Chronic Widespread Pain

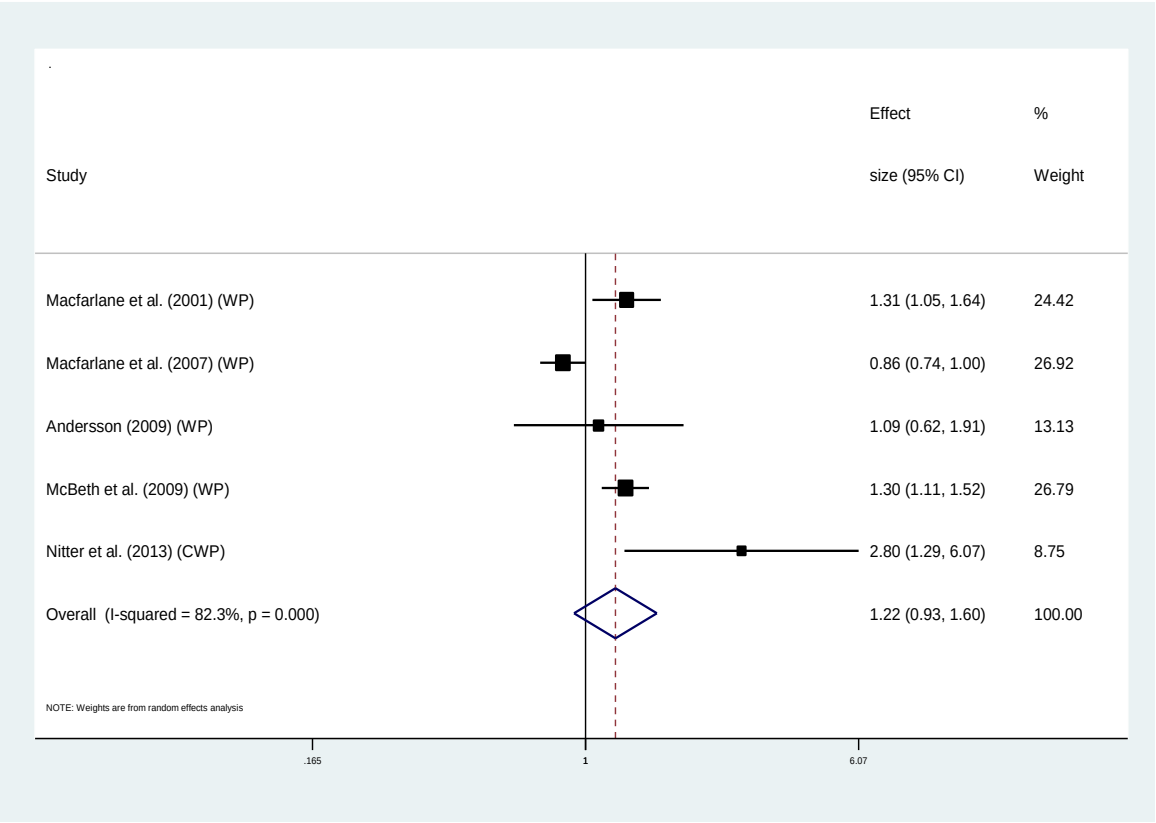


Figure 2.3 Forest plot of the association between chronic widespread pain and all-cause mortality in identified studies (effect sizes are MRR only)

MRR=Mortality Rate Ratio, CI= Confidence Interval, WP = Widespread Pain, CWP = Chronic Widespread Pain

Cause specific mortality

Eight of the studies provided information regarding cause specific mortality (Andersson, 2009; Dreyer et al., 2010; Macfarlane et al., 2007; Macfarlane et al., 2001; McBeth et al., 2009; Smith et al., 2003; Torrance et al., 2010; Wolfe, Hassett, et al., 2011) (Table 2.1). Five of these used MRRs and could be combined to provide pooled estimates. For cancer (Figure 2.4), the MRRs ranged from 0.64 to 2.07 (I^2 = 85.3%), pooled estimate MRR 1.20; 95% CI 0.74, 1.93 (p=0.459). For the sub-group of studies measuring widespread pain and cancer mortality (Figure 2.5) MRRs ranged from 0.64 to 2.07 (I^2 = 87.9%), pooled estimate MRR 1.29; 95% CI 0.70, 2.39 (p=0.417). For cardiovascular disease mortality (Figure 2.6), the MRRs ranged from 0.83 to 2.17 (I^2 =72.5%) pooled estimate MRR 1.09; 95%CI 0.84,

1.41 (p=0.536). In the widespread pain subgroup (Figure 2.7) the MRRs ranged from 0.83 to 2.17 (I^2 = 76.8%), pooled estimate MRR 1.17; 95% CI 0.85, 1.63 (p=0.338). Only four studies provided information about respiratory disease mortality (Figure 2.8). The effect sizes ranged from 0.89 to 1.23 (I^2 = 0.0%), pooled estimate MRR 1.01; 95%CI 0.78, 1.30) (p=0.944). For the widespread pain subgroup (Figure 2.9) the MRRs ranged from 0.89 to 1.01 (I^2 = 0.0%), pooled estimate MRR 0.97; 95% CI 0.73, 1.28 (p=0.817). Of the studies not included in the meta-analysis, only one study reported an increased risk of mortality from one of these three main causes of death was Smith and colleagues (2003) who reported an increased risk of respiratory disease mortality for women with chronic pain (AOR 2.22; 95%CI 1.1, 4.39).

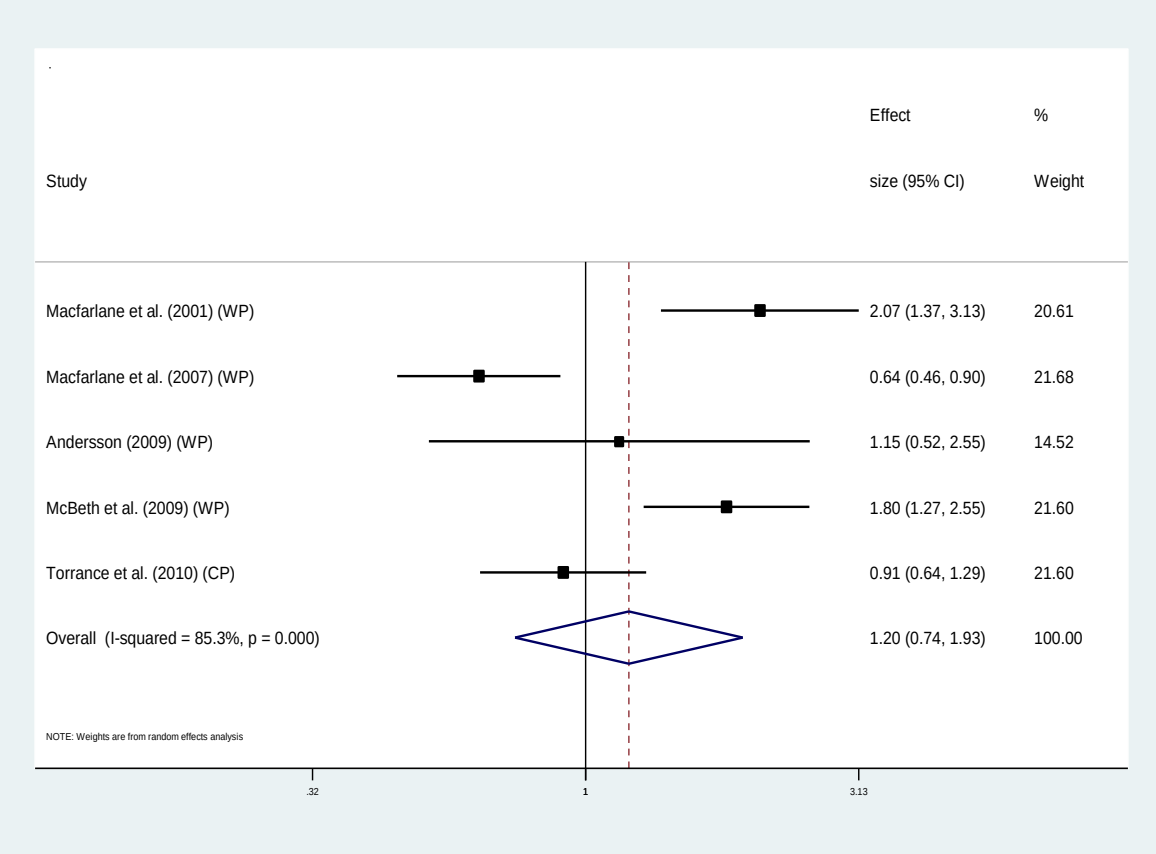


Figure 2.4 Forest plot of the association between chronic pain and cancer mortality in identified studies (MRR only)

MRR=Mortality Rate Ratio, CI= Confidence Interval, WP = Widespread Pain, CP=Chronic Pain

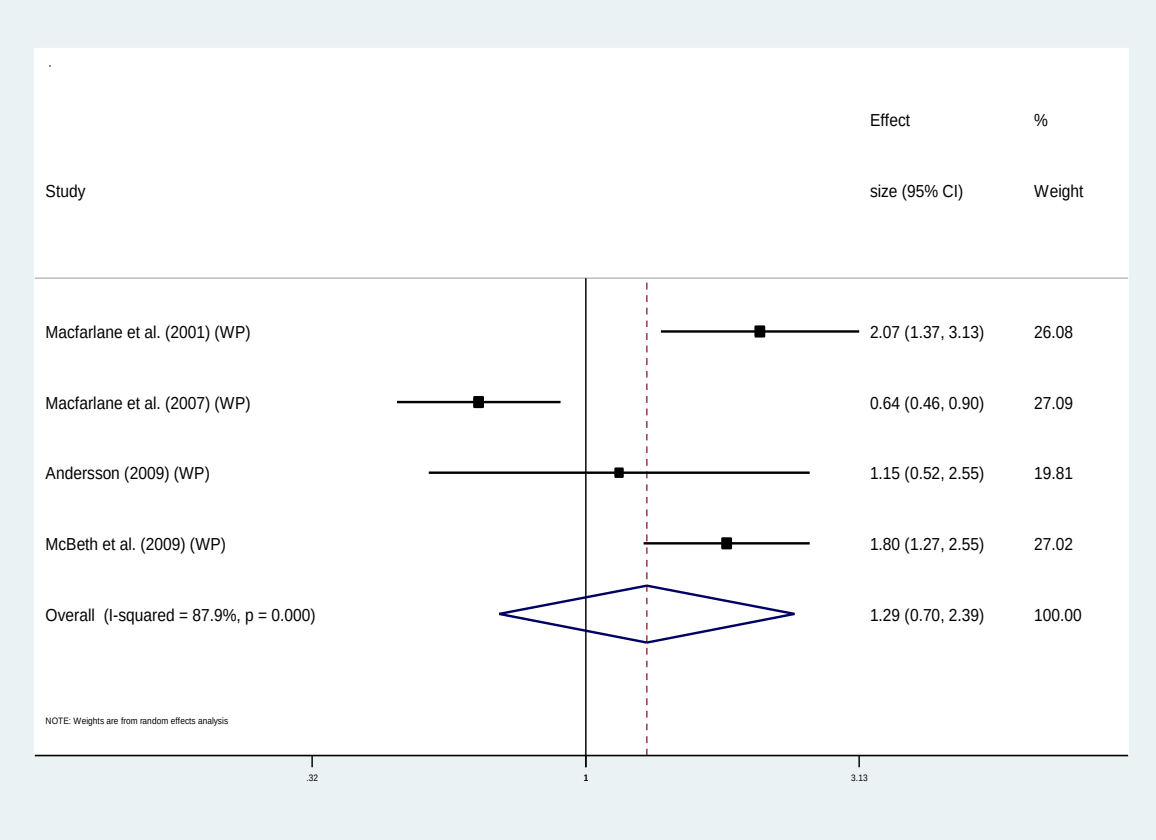


Figure 2.5 Forest plot of the association between chronic widespread pain and cancer mortality in identified studies (MRR only)

MRR=Mortality Rate Ratio, CI= Confidence Interval, WP = Widespread Pain, CP=Chronic Pain

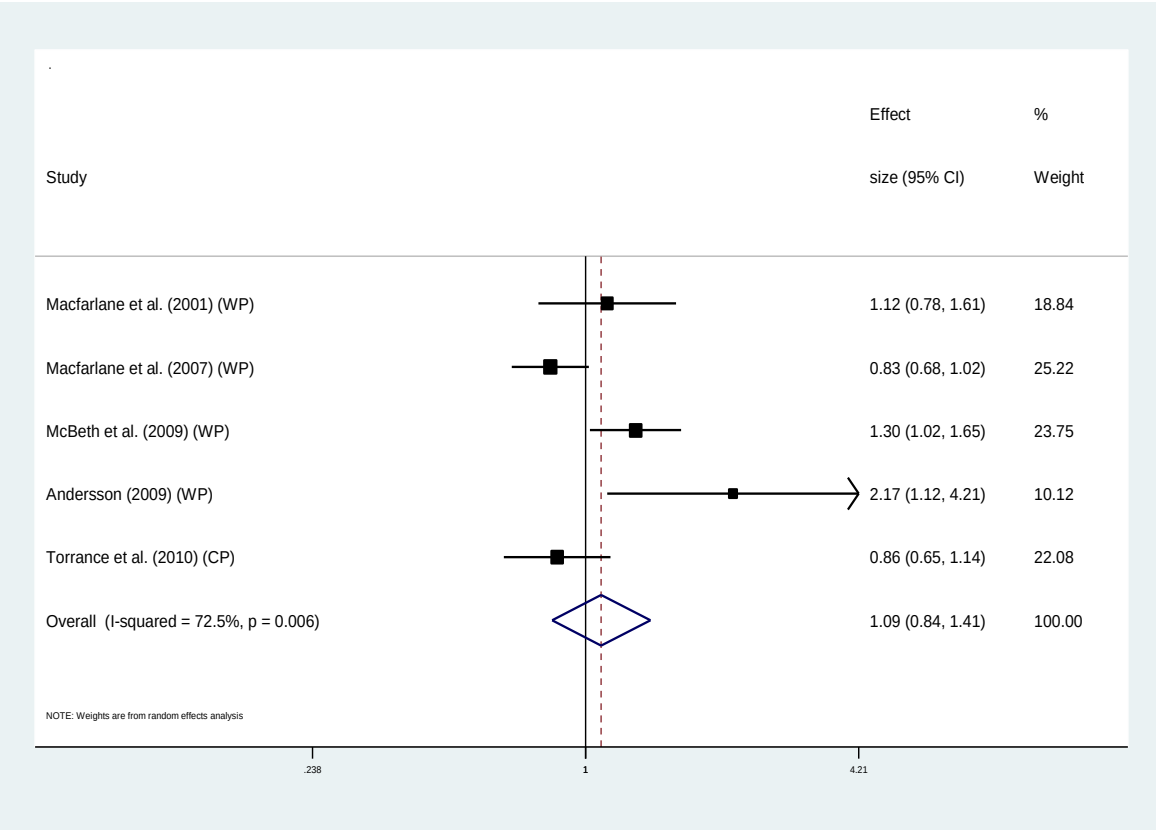


Figure 2.6 Forest plot of the association between chronic pain and cardiovascular disease mortality in identified studies (MRR only)

MRR=Mortality Rate Ratio, CI= Confidence Interval, WP = Widespread Pain, CP=Chronic Pain

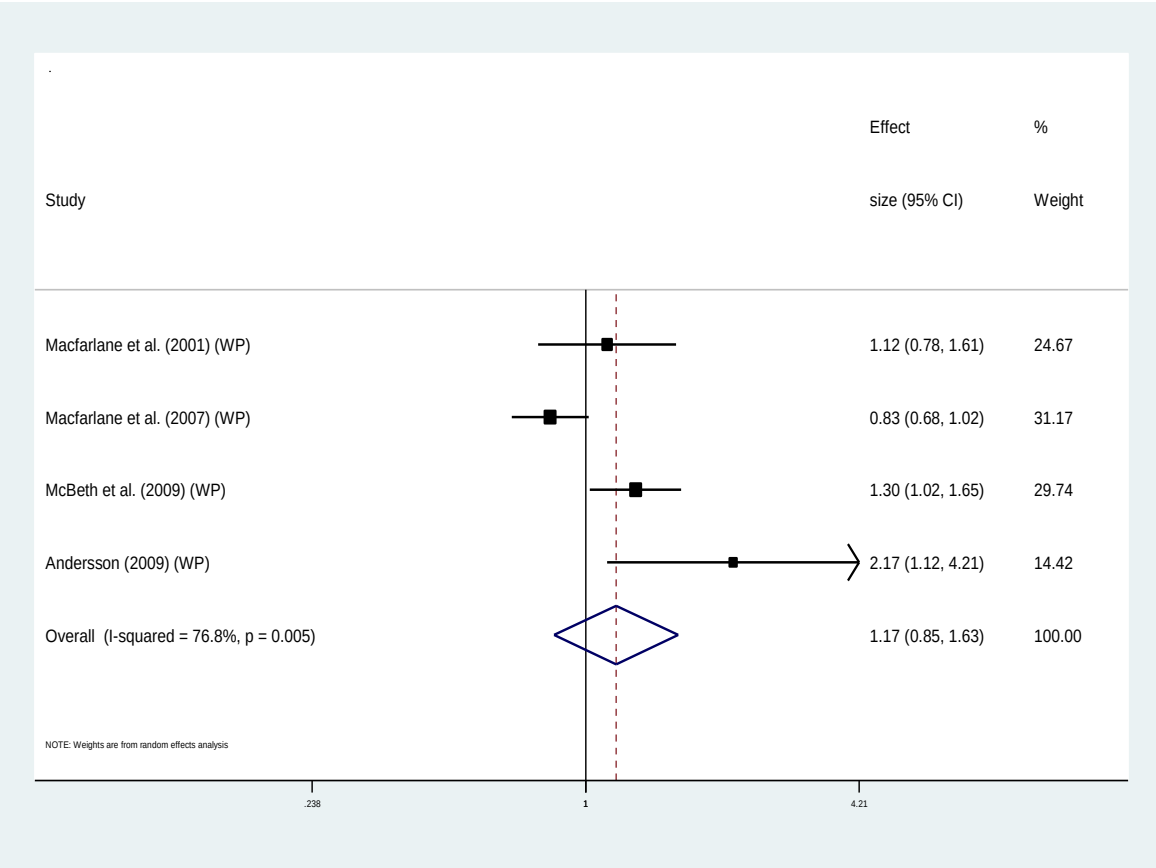


Figure 2.7 Forest plot of the association between chronic widespread pain and cardiovascular disease mortality in identified studies (MRR only)

MRR=Mortality Rate Ratio, CI= Confidence Interval, WP = Widespread Pain

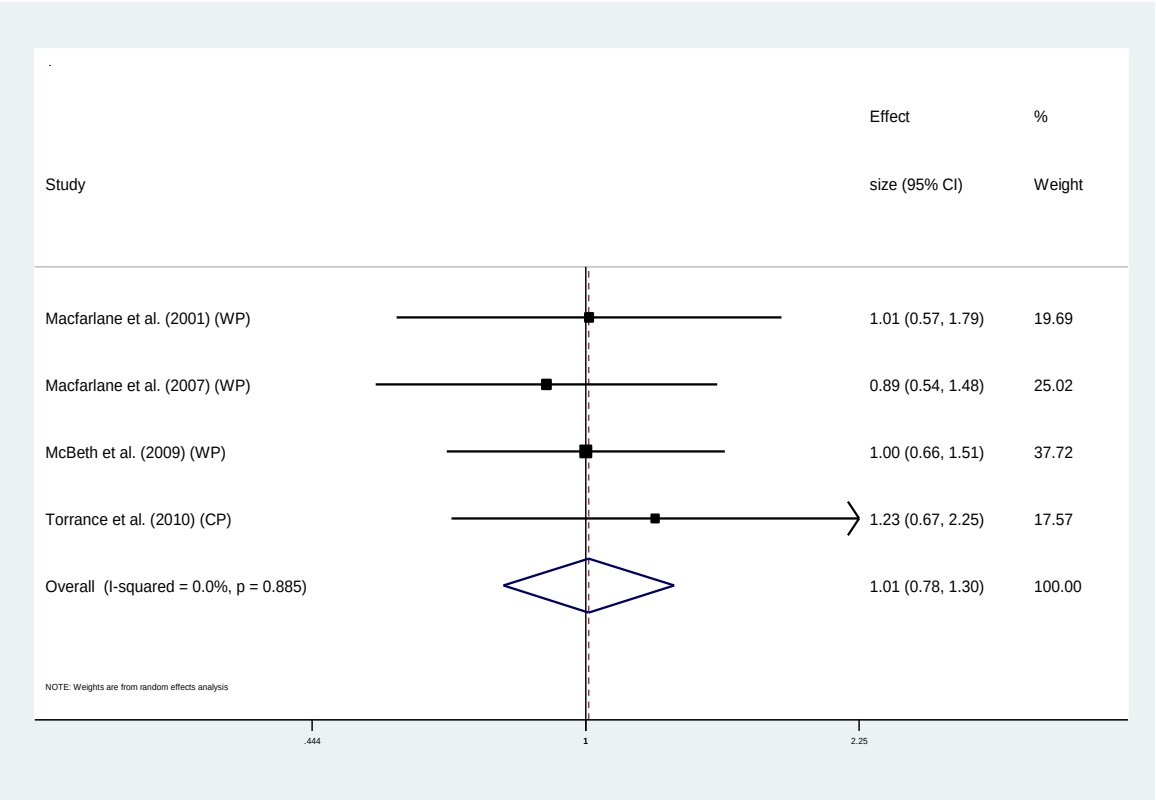


Figure 2.8 Forest plot of the association between chronic pain and respiratory disease mortality in identified studies (MRR only)

MRR=Mortality Rate Ratio, CI= Confidence Interval, WP = Widespread Pain, CP=Chronic Pain

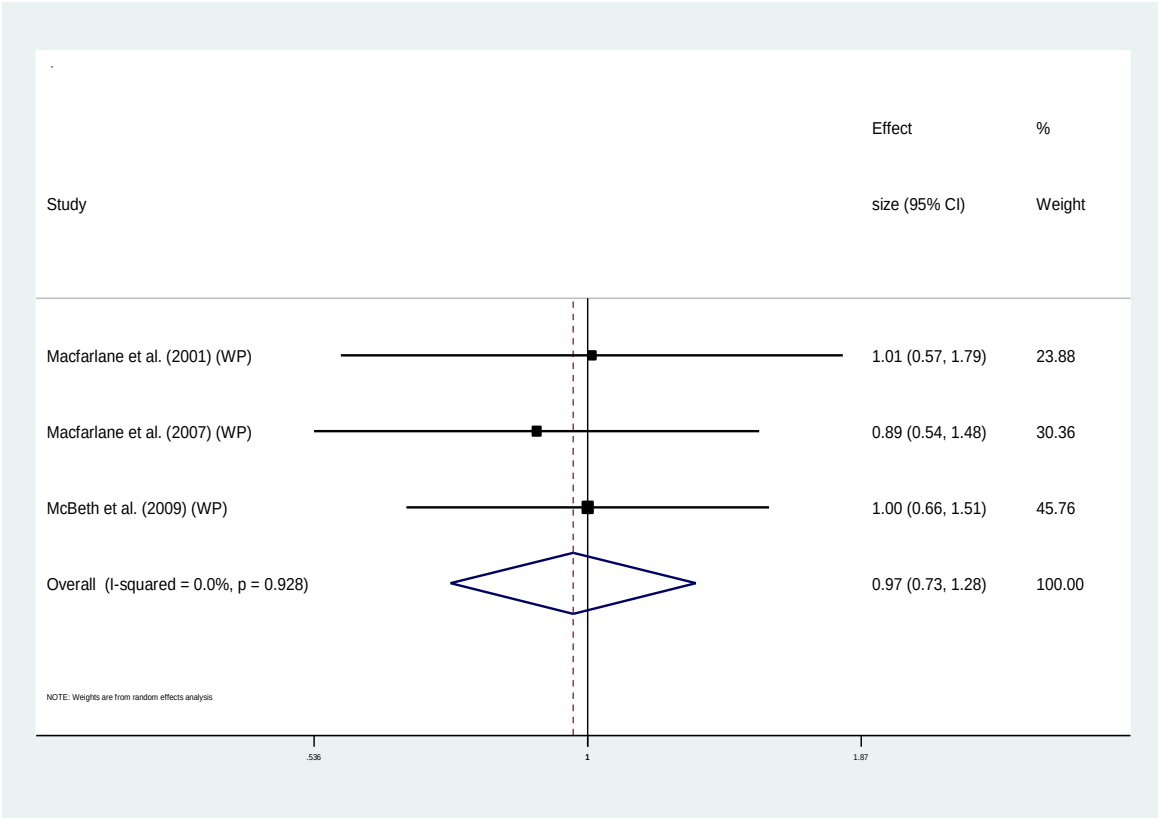


Figure 2.9 Forest plot of the association between chronic widespread pain and respiratory disease mortality in identified studies (MRR only)

MRR=Mortality Rate Ratio, CI= Confidence Interval, WP = Widespread Pain

2.6.5 Evidence synthesis: narrative review of potential sources of heterogeneity

The high heterogeneity between studies may be explained by the small number of identified studies and differences in the age and sex distribution of study samples, follow-up time, pain phenotype, population characteristics, methods of analysis and potential confounding factors included (Table 2.3).

Age and sex distribution

The age and sex distribution of the study samples varied between studies however there were no clear differences in the results that could be attributed to this. The meta-analysis was conducted using results which were adjusted for age and sex limiting the influence of these factors on the observed heterogeneity.

Follow up time

Follow up time varied between studies (see Table 2.3) ranging from 6 years (Smith et al., 2003) to 35 years (Wolfe, Hassett, et al., 2011). Length of follow-up was not clearly associated with the differences in findings between studies (e.g. longer follow up periods were no more likely to be associated with significant mortality risks).

Pain phenotype

All of the studies which examined links with widespread pain reported how closely their phenotype adhered to the criteria proposed by the American College of Rheumatology (ACR) in 1990, (Wolfe et al., 1990) however there were inconsistencies between studies (see Table 2.1). The least stringent definition of widespread pain was applied by Macfarlane and colleagues (2007) who did not find an association between widespread pain and mortality (Macfarlane et al., 2007).

Table 2.3 Summary of main sources of heterogeneity between the included studies in the systematic review							
Study	**Pain phenotype**	**Age**	**Location**	**Gender distribution (% female)**	**Follow-up**	**Outcome (all-cause mortality)**	**Factors adjusted for**
Macfarlane, G.J. et al. (2001)	WP	18-85years	North West England	58%	8yrs	**MRR (95%CI)** Adjusted 1.31 (1.05-1.65)	age, sex, study location
Macfarlane, G.J. et al. (2007)	WP	30 years and over	Finland	54%	14-16yrs	**MRR (95%CI)** Adjusted 0.86 (0.74-1.00)	age, gender, education, physical work stress, mental work stress, alcohol consumption, tobacco smoking, BMI
Andersson, H.I. (2009)	WP	25-74 years	Sweden	50%	14 yrs	**MRR (95%CI)** Crude 1.95 (1.26-3.03) Adjusted 1.09 (0.62-1.90)	Age, sex, living alone, contact with friends, club membership, chronic disease, smoking, physical activity, perception of stress, BMI, insomnia
McBeth, J. et al. (2009)	WP	16 years and over	North West England	51.6%	8.2yrs	**MRR (95%CI)** Crude 2.4 (1.9-2.9) Adjusted 1.3 (1.1-1.5)	age, sex, practice, ethic group, Townsend score of deprivation
Sjøgren P. et al. (2010)	CP	16 years and over	Denmark	51.3%	8 yrs	**MRR (95%CI)** Adjusted 1.21 (1.02-1.44)	age, sex, education, marital status, BMI, smoking, antidepressant use, anxiolytic use, self-reported circulatory diseases, infectious or parasitic diseases, diabetes and mental disorders
Torrance N. et al. (2010)	CP	Mean 58.43 years	North East Scotland	52.7%	10 yrs	**MRR (95%CI)** Crude 1.32 (1.14-1.54) Adjusted 0.90	age, sex, education, housing, long term limiting illness

						(0.74-1.07)	
Nitter A.K. & Forseth K.Ø. (2013)	CWP	20 -68 years	Arendal, Norway	100%	18 yrs	**MRR (95%CI)** Adjusted 2.8 (1.3-6.1)	age, sleep problems, feeling anxious, frightened or nervous, number of non-specific health complaints
Dreyer, L. et al. (2010)	FM	19 years and over	Denmark	94%	15 yrs (Mean 3.9 years)	**SMR (95%CI)** 1.25 (0.9-1.7)	Standardised to Danish population (according to age, sex, calendar month)
Wolfe, F. et al. (2011)	FM	Mean 50.5 years, (SD 12.4)	USA	94%	35yrs (Mean 7.3 years)	**SMR (95%CI)** 0.90 (0.61-1.26)	Standardised to U.S. population (according to age, sex, calendar month)
Smith, B.H. et al. (2003)	CP	42-81 years	UK	100%	6 years	**AOR (95%CI)** 1.1 (0.81-1.26)	age, social class, smoking

WP = Widespread Pain, CP = Chronic Pain, CWP = Chronic Widespread Pain, FM = Fibromyalgia
MRR = Mortality Rate Ratio
SMR = Standardised Mortality Ratio
AOR = Adjusted Odds Ratio
CI = Confidence Interval

In contrast, the three studies that defined widespread pain similar to the ACR 1990 definition (Andersson, 2009; Macfarlane et al., 2001; McBeth et al., 2009) did report an association between widespread pain and mortality. Nitter and Forseth (2013) who were able to determine chronic widespread pain in all participants reported the strongest association with increased risk of mortality after adjusted analyses (Nitter & Forseth, 2013). Differences in pain phenotype were explored in the sensitivity analysis in the meta-analysis, where a slight increase in the pooled estimate was observed when the analysis was restricted to widespread pain for all-cause mortality (1.22 cf 1.14), cancer mortality (1.29 cf 1.20) and cardiovascular disease mortality (1.17 cf 1.09) but not respiratory disease mortality (0.97 cf 1.01).

Population characteristics

The study settings were heterogeneous. Four of the studies were carried out in the UK (Macfarlane et al., 2001; McBeth et al., 2009; Smith et al., 2003; Torrance et al., 2010), two in Denmark (Dreyer et al., 2010; Sjøgren & Grønbæk, 2010), one in Finland (Macfarlane et al., 2007), one in Sweden (Andersson, 2009), one in Norway (Nitter & Forseth, 2013) and one in the USA (Wolfe, Hassett et al., 2011). A greater proportion of the participants in the Macfarlane and colleagues (2007) study lived in rural settings (Macfarlane et al., 2007) compared to the Macfarlane and colleagues (2001) and the McBeth and colleagues (2009) studies which although different cohorts, were both carried out in the same urban area of the UK (Macfarlane et al., 2001; McBeth et al., 2009). These two studies in the urban area reported an increased risk of mortality for people with widespread pain and an increased risk of cancer mortality which were not supported by the study in a rural setting (Macfarlane et al., 2007).

Eight of the studies were carried out in population cohorts (Andersson, 2009; Macfarlane et al., 2007; Macfarlane et al., 2001; McBeth et al., 2009; Nitter & Forseth, 2013; Sjøgren & Grønbæk, 2010; Smith et al., 2003; Torrance et al., 2010) and two were clinical cohorts (Dreyer et al., 2010; Wolfe, Hassett, et al., 2011). Both clinical cohorts reported no significant increased risk of mortality for fibromyalgia patients.

Adjustment for potential confounders

There was wide variability in the type and number of potential confounders adjusted for between studies. Only three of the studies reported crude results (Andersson, 2009; McBeth et al., 2009; Torrance et al., 2010), all indicating a significant association between chronic or widespread pain and mortality. It was difficult to determine if potential confounders consistently explained the relationship between chronic pain and mortality. Andersson (2009) measured and adjusted for the highest number of potentially confounding factors (see Table 2.3 for details) and concluded their observed increased risk of mortality for people with widespread pain could be explained by lifestyle factors such as smoking and physical inactivity together with reported stress and disturbed sleep (Andersson, 2009). McBeth and colleagues (2009), and Nitter and Forseth (2013) did not include any lifestyle factors in their analyses and the increased risk of mortality observed in these studies was robust to adjustment for the factors they included (see Table 2.1) (McBeth et al., 2009; Nitter & Forseth, 2013). However, Torrance and colleagues (2010) reported the association between chronic pain and mortality attenuated to non-significance following adjustment without including lifestyle factors (Torrance et al., 2010) (Table 2.3).

2.7 Discussion

2.7.1 Summary of findings

The results of this systematic review and meta-analysis suggested that there was a modest relationship between chronic pain and increased mortality but this was not significant. The results also suggested this relationship may be explained by cancer mortality. Confidence in these findings is restricted due to the small number of included studies and heterogeneity between them. Restricting the analysis to studies measuring widespread pain and mortality resulted in an increase in the size of the pooled estimates for all-cause, cancer and cardiovascular disease mortality but these were also non-significant.

Very few studies have examined the relationship between chronic pain and mortality. Only three studies reported crude results, all of which suggested there was an association between chronic or widespread pain and an increased risk of all-cause mortality (Andersson, 2009; McBeth et al., 2009; Torrance et al., 2010). However adjustment for confounders led to attenuation of the relationship. This suggests that adults with chronic or widespread pain have an increased mortality rate which is to some extent explained by socio-demographic and lifestyle factors, however the low number of studies and high heterogeneity again reduces the certainty of this. Significant associations between chronic or widespread pain and increased risk of mortality from cancer, cardiovascular disease, cerebrovascular disease, liver cirrhosis, suicide, accidents, influenza and pneumonia, septicaemia were reported in single studies.

2.7.2 Differences between studies

The differences between the ten studies led to high levels of heterogeneity. The study populations differed on a number of characteristics which will have contributed to the variance in prevalence rates of widespread pain and mortality, and the relationship between them.

Definition of chronic or widespread pain

Information regarding the location of pain was lacking in three of the included studies so the presence of widespread pain could not be confirmed although chronic pain often occurs in multiple sites (Carnes et al., 2007). Similarly, details regarding the chronicity of pain were not available in all studies measuring widespread pain but in 80-90% of persons reporting widespread pain, the pain has been present for more than three months (Macfarlane et al., 2001). Although this means a small proportion of participants may have been misclassified it would also lead to an underestimation of the true effect. More rigorous definitions of widespread pain were more strongly associated with mortality. In additional analysis, Wolfe et al. (2011) reported that within those with fibromyalgia, those satisfying the more stringent ACR 2010 criteria (Wolfe et al., 2010) had an increased risk of mortality than those who did not meet the new criteria but met the 1990 criteria (HR 1.62; 95%CI 1.19, 2.21) (Wolfe et al., 2011). The ACR 2010 criteria extended the scope of defining widespread pain beyond the location of pain by including an assessment of the severity of accompanying symptoms (Wolfe, Clauw, et al., 2011). Increased severity and duration of pain, in addition to extent, increases the risk of mortality (Tang & Crane, 2006; Torrance et al., 2010). The revised ACR 2010 criteria, which can be measured using

self-report tools in epidemiological and clinical studies, offers the potential to harmonise definitions of widespread pain in future studies (Wolfe, Clauw, et al., 2011).

Methods of analysis

There were differences in the reference group between studies which prevented clear comparisons. Eight studies used participants with no pain as the reference group and two used standardised populations, one in Denmark (Dreyer et al., 2010) and one in the US (Wolfe, Hassett, et al., 2011) which include people both with and without pain. In an additional analysis, Wolfe and colleagues (2011) compared mortality rates between fibromyalgia and osteoarthritis patients and reported no significant difference (Wolfe, Hassett, et al., 2011). Mortality risk is higher in those with osteoarthritis compared to the general population (Hochberg, 2008) therefore this finding is not comparable to the mortality rate ratios used in other studies. The comparison group (osteoarthritis patients) cannot be considered analogous to a no pain group.

Different methods of analysis were used to calculate the outcome measures (SMR, MRR and AOR) due to variations in reference groups. Sufficient data were not available to enable conversion to comparable outcome measures for all studies. The effects of these different analysis techniques is demonstrated by McBeth et al (2009), who reported a 30% increased risk of mortality for people with widespread pain compared to a no pain group but when compared to the mortality rate for North West England mortality risk was lower and not significant (SMR 1.14; 95%CI 0.99, 1.30) (McBeth et al., 2009). The more similar the reference group, the less likely a relationship will be observed. Where the comparison is with a standardised population the reference group will include participants with and without pain. Use of general population cohorts in which a no-pain

group can be identified will allow for a sharper contrast between a group most at risk (those with widespread pain) with those least at risk (those with no pain).

Follow-up time

Variations in follow-up time between studies may influence mortality rates although this was not clear from this review. The mortality rate in those with pain has been shown to be higher in the earlier periods of follow-up (Jordan & Croft, 2010). Jordan and colleagues (2013) have also demonstrated the strength of associations between pain in different musculoskeletal sites and cancer diminished with time indicating pain may be a marker of rather than a cause of cancer (Jordan, Hayward, Blagojevic-Bucknall, & Croft, 2013). However, McBeth et al., (2009) reported no change in the relationship between widespread pain and both cancer and cardiovascular death after excluding participants who had died in the first year of follow up (McBeth et al., 2009). Standard periods of follow-up, allowing both short and long term assessment of risk would enable comparisons between studies and allow a more accurate picture of the relationship to be determined.

Mechanisms

Differences in study setting may contribute to variations in factors associated with the presence of pain and mortality. Pain experienced by those in rural settings may be more likely to be related to physical labour than those in urban settings (McBeth et al., 2009), although this may mean they are more physically active. Physical activity is known to reduce the risk of chronic diseases and premature death (Warburton, Nicol, & Bredin, 2006). Clinical and population cohorts will also have different characteristics of pain, health and socio-demographic factors. Depending on how healthcare is accessed, the

clinical cohorts may have more severe symptoms and comorbidities compared to general population samples, which will impact on mechanisms to and rates of mortality. Wolfe and colleagues (2011) report that the fibromyalgia patients in their study may have higher socioeconomic status than the general population as the majority had medical insurance and received care from specialists rather than general physicians (Wolfe, Hassett, et al., 2011). Higher socioeconomic status and access to care are associated with survival and may explain why no relationship between fibromyalgia and mortality was found in these studies (Alter, Naylor, Austin, & Tu, 1999).

The studies included in this review treated covariates as confounders and adjusted for them in their analyses. Information regarding the relative contribution of individual confounders to the models was not available. However, it may be that these factors are instead moderating or mediating the relationship between pain and mortality. Simply adjusting for such factors may lead to spurious associations between predictor and outcome (Greenland, Pearl, & Robins, 1999). Adjustment for confounders in the ten studies, such as age, sex, socio-demographic status and lifestyle factors, indicated that they had a role in the relationship between widespread pain and mortality. Comparing similarly adjusted results will control for some of the variance in the associations between studies due to different population characteristics (e.g. differences in age and sex distributions). However differences in how these factors were measured and classified will have contributed to the heterogeneity. For example, one study used the Townsend score of deprivation as a measure of socioeconomic status; this is an area-level measure which is derived from variables representing unemployment, overcrowding within households, non-home ownership and lack of car ownership (McBeth et al., 2009). In

contrast the other studies included individual level measures of socio-economic status, such as educational attainment and owning medical insurance (Wolfe, Hassett, et al., 2011).

There were substantial differences in the number of additional factors measured and adjusted for between studies (Table 2.3). Notably the significant relationship reported in the crude analysis by Andersson and colleagues (2009) attenuated and was no longer significant when adjusted for living alone, contact with friends, club membership, comorbidity, smoking, physical activity, BMI, perception of stress and insomnia (Andersson, 2009) indicating possible pathways between pain and mortality. Pain is associated with depression, obesity, a reduction in physical activity (Ray, Lipton, Zimmerman, Katz, & Derby, 2011) and smoking motivation (Ditre & Brandon, 2008). Wolfe et al., (2011) found BMI and smoking to be significant predictors of mortality in a sub-section of participants (Wolfe, Hassett, et al., 2011). Many of the diseases where increased mortality was observed have links to lifestyle factors. Cancer and cardiovascular disease are associated with reduced physical activity (Warburton et al., 2006) and cancer with smoking (Fagerström, 2002). A follow up to the Macfarlane and colleagues (2001) study using the same cohort reported the association they observed was with both cancer incidence and survival; specifically with breast and prostate cancers (McBeth et al., 2003), both of which have been shown to be associated with physical inactivity (Liu et al., 2011; Monninkhof et al., 2007).

Consideration of mechanisms between pain and mortality with the appropriate designation of potential mediators and moderators rather than confounders would

further the understanding of any relationship between pain and mortality. Such analysis would identify potentially modifiable targets to reduce an increased risk of mortality. There are a number of potential mediators and moderators that were not considered in the identified studies in this review which are associated with both pain and mortality, such as anxiety and depression (Bair & Robinson, 2003; Mykletun et al., 2009) social participation and social isolation (House, 2001; Moulin, Clark, Speechley, & Morley-Forster, 2002) and fatigue (Fishbain, Cole, & Cutler, 2003; Hardy & Studenski, 2008). Examination of their potential role in the link between pain and mortality may identify novel targets for healthcare to reduce impact.

2.7.3 Strengths and limitations

There were a number of strengths in this current study. A systematic approach was undertaken to maximise the chances of identifying all relevant studies of chronic pain and mortality. The quality of the identified studies was assessed using an established appraisal tool designed to focus on potential bias within studies (Hayden et al., 2006). Agreement between reviewers of the risk of bias was high (Table 2.2). Including papers written only in English may be one weakness and it is possible some relevant findings may have been missed. However an additional more recent search of CINAHL, Medline and EMBASE did not find any relevant non-English studies.

The small number of studies ($k<20$) means that I^2 values should be interpreted with caution as there is little power to detect true heterogeneity and as such any pooled calculation of effect may be misleading (Huedo-Medina, Sánchez-Meca, Marín-Martínez, & Botella, 2006). A more complex meta-analysis could have been undertaken to include the studies with multiple follow-ups and account for the correlation between them.

However, even with a greater number of studies, there is general concern regarding the appropriateness of the use of meta-analyses in reviews of observational studies due to the likelihood for high heterogeneity as a result of difficulties in overcoming selection and confounding biases common to this type of study (Dickersin, 2002). The estimates of pooled effects calculated in meta-analyses of observational studies are likely to be flawed and it is therefore more useful to have an assessment of the potential sources of heterogeneity as the focus of such systematic reviews (which has been included here) rather than a statistical combination of the data (Egger et al., 2001).

2.7.4 Implications for research

This review indicated a modest association between chronic and widespread pain and increased mortality, particularly cancer mortality but further research is needed to confirm this. Even a small increased risk of cancer mortality is significant when it applies to a large proportion of the population (Crombie, 2001). The findings of this systematic review indicate lifestyle factors may have an important role in the association between pain and mortality and these may be specific to particular conditions (McBeth et al., 2003). As previously discussed, research to identify potential mechanisms of a relationship between pain and mortality in the general population where specific mediators and moderators can be assessed using appropriate statistical methods could direct future interventions to reduce pain impact. Attention should also be given to previously unmeasured lifestyle, health, social and psychological factors.

2.8 Potential pathways from pain to mortality

Lifestyle, health, social and psychological factors may explain the link between pain and mortality and may identify potential targets for interventions or populations who are particularly vulnerable and would benefit from prevention strategies. The following section outlines potential mediators of the link between pain and mortality; this thesis will go on to describe the empirical analysis used to determine whether these factors mediate the relationship between pain and mortality. The proposed mediating factors were selected based on their theoretical plausibility as mediators and the availability of data to test this using the databases described in Chapter Four.

2.8.1 Lifestyle factors

Pain is associated with and predicts an increase in harmful lifestyle factors which are linked with increased mortality. Examples of lifestyle factors (i.e. health related behaviours or the potential results of those behaviours (van Hecke, Torrance, & Smith, 2013)) associated with pain are physical inactivity (McBeth & Nicholl, 2010), smoking (Ditre & Brandon, 2008), obesity (Heim, Snijder, Deeg, Seidell, & Visser, 2008), sleep problems (Moldofsky, 2001) and alcohol consumption in men (Leveille et al., 2005).

Physical inactivity

The WHO defines physical activity as "any bodily movement produced by skeletal muscles that requires energy expenditure" (WHO website, 2015). Levels of physical activity are lower in people with pain often as a result of physical limitation (Kamaleri et al., 2008; McBeth & Nicholl, 2010; Vogt, Lauerman, Chirumbole, & Kuller, 2002). While there is concern that strenuous activity may cause some musculoskeletal problems, there is

consistent evidence that regular moderate physical activity can reduce the persistence of pain and improve pain related function (Croft et al., 2010; Dugan et al., 2009).

Physical inactivity has been reported to be the fourth leading global risk factor for mortality, accounting for approximately 3.2 million deaths each year (WHO website, 2015). Frequent physical activity is protective against the development of chronic diseases such as cardiovascular disease, diabetes, cancer, hypertension, obesity, osteoporosis, depression and premature death (Warburton et al., 2006). Physical activity helps to improve bodily movement, reduce fatigue, control weight and enhance the immune system (Liu et al., 2011). Biological mechanisms responsible for the health benefits associated with physical activity include reduced abdominal adiposity and improved weight control, reduced triglyceride levels, increased high density lipoprotein (HDL) cholesterol levels and decreased low-density lipoprotein (LDL)-to-HDL ratios, improved glucose homeostasis and insulin sensitivity, reduced blood pressure, improved autonomic tone, reduced systemic inflammation; decreased blood coagulation, improved coronary blood flow, strengthened cardiac function and enhanced endothelial function (Warburton et al., 2006). The empirical analysis described in this thesis tested the hypothesis that pain would lead to increased mortality through physical inactivity.

Smoking

Cigarette smoking is one of the ten leading risk factors for death worldwide (Gellert, Schottker, & Brenner, 2012). Compounds contained in cigarette smoke produce significant physiological effects, many of which are detrimental to health (Shi, Weingarten, Mantilla, Hooten, & Warner, 2010). Smoking increases the risk of developing a large number of diseases including cancer of the lung, oesophagus, bladder, kidney and

stomach, chronic obstructive pulmonary disease (COPD), coronary heart disease, stroke, peripheral vascular disease and peptic ulcer disease (Doll, Peto, Boreham, & Sutherland, 2004; Fagerström, 2002) and is associated with the presence of chronically painful conditions such as fibromyalgia, rheumatoid arthritis and chronic musculoskeletal pain (Ditre & Brandon, 2008; Zvolensky, McMillan, Gonzalez, & Asmundson, 2010).

The pain-inhibiting effect of smoking through the analgesic properties of nicotine (Shi et al., 2010) supports the notion that some pain sufferers use smoking as a way of coping with their pain therefore pain is a motivator of smoking behaviour (Ditre & Brandon, 2008). It was hypothesised that a link between pain and mortality would exist via smoking behaviour.

Alcohol consumption

Alcohol consumption may explain a relationship between pain and mortality. Excessive alcohol consumption is associated with the development of and death from liver cirrhosis (Rehm et al., 2010). Dreyer and colleagues (2010) reported increased mortality due to liver cirrhosis in fibromyalgia patients which suggests a pathway between pain and mortality via increased alcohol consumption (Dreyer et al., 2010). However, the relationship between pain and alcohol consumption is unclear. People experiencing pain may use alcohol as a way of coping with their pain; the use of alcohol for medicinal purposes is common in older people (Aira, Hartikainen, & Sulkava, 2008). However, alcohol consumption is often lower in people with pain (Brennan, Schutte, SooHoo, & Moos, 2011; McBeth & Nicholl, 2010). This is partly consistent with the findings of Leveille et al., (2005) who observed that both men and women with widespread pain reported the lowest alcohol consumption, but men with single or multi-site pain were more likely

to consume higher amounts of alcohol than men without pain (Leveille et al., 2005). Brennan and colleagues (2011) reported an association between more painful conditions and greater negative effects of alcohol consumption (e.g. physical or psychological problems or social conflicts) in men but not women indicating men and women respond differently to painful symptoms (Brennan et al., 2011). It was hypothesised pain would lead to mortality via increased alcohol consumption but this relationship would be stronger in males compared to females.

Obesity

Obesity is an increasing health problem worldwide (WHO website, 2015b). It is commonly identified from an individual's body mass index (BMI) which is determined by dividing the weight of a person in kilograms by the square of their height in metres. Typically people with a BMI of above 30 are considered to be obese (WHO website, 2015b). Obesity is associated with an increased risk of mortality (Flegal, Kit, Orpana, & Graubard, 2013). This is likely due to the health risks associated with increased BMI including metabolic syndrome, hypertension, type 2 diabetes, coronary artery disease and stroke, respiratory problems, cancer, reproductive problems, osteoarthritis and liver and gall bladder disease (Kopelman, 2007). Obesity is also associated with low back pain, tension type headache or migraine, abdominal pain, chronic widespread pain and fibromyalgia (Johnson Wright et al., 2010), pain when standing, moving position, sitting, walking, and "unbearable" or "constant" pain (Heim et al., 2008) and work restricting musculoskeletal pain (Peltonen, Lindroos, & Torgerson, 2003). It was hypothesised that the impact of pain on mortality could be explained through its link with increased levels of obesity. Notably like pain, the impact of obesity is likely to be through additional mediators or explanatory factors (for example, cardiovascular disease).

Sleep problems

Sleep is comprised of highly organised, complex physiological processes which are imperative for maintaining health (Luyster, Strollo, Zee, & Walsh, 2012). Excessive and reduced sleep is associated with mortality (Cappuccio, D'Elia, Strazzullo, & Miller, 2010). Reduced sleep (less than 6 hours) may contribute to cardiovascular disease, diabetes and obesity through impaired glucose tolerance, higher evening cortisol levels, alterations in sympathetic nervous system activity, reduced leptin levels (which regulates satiety), increased levels of ghrelin (which regulates hunger), increases in inflammatory markers such as C-reactive protein and interleukin (IL)-6 (Luyster et al., 2012). The reason for an association between mortality and excessive sleep is uncertain but may be explained by depression, undiagnosed illness or physical inactivity (Patel, Malhotra, Gottlieb, White, & Hu, 2006).

The relationship between pain and sleep is reciprocal; pain can lead to sleep problems and sleep problems can exacerbate pain problems (Moldofsky, 2001). Duration of sleep can predict pain report; less than 6 or more than 9 hours of sleep has been shown to be associated with greater pain the next day (Edwards, Almeida, Klick, Haythornthwaite, & Smith, 2008). It was hypothesised that pain would lead to sleep problems which would then lead to increased mortality.

2.8.2 Health factors

Pain is associated with and predicts poor health (Blyth et al., 2015; Dominick, Blyth, & Nicholas, 2012; Goldberg & McGee, 2011). The World Health Organisation (WHO) defines health as "a state of complete physical, mental and social wellbeing and not merely the absence of disease and infirmity" (WHO, 1948). For the purposes of this study the

secondary definition of health being “the extent to which an individual can realize aspirations, satisfy needs and change or cope with the environment” (WHO, 1984) is utilised to reflect functional ability. The association between pain and poor physical function increases with increasing pain severity (Landi et al., 2009, Ang, Kroenke, & McHorney, 2006) and number of pain sites (Kamaleri et al., 2008), and the prevalence of pain that interferes with life increases with age (Thomas et al., 2007). Pain also leads to a reduction in perceptions of general heath (Reyes-Gibby, Aday, & Cleeland, 2002) and this is an important determinant of health outcomes and mortality (Idler & Benyamini, 1997).

Self-rated health

Pain predicts poor self-rated health (Reyes-Gibby et al., 2002). Self-rated health is an individual’s aggregated reflection of the many dimensions that affect health (Idler & Benyamini, 1997; Jylhä, 2009). These include the evaluation of multiple illnesses and symptoms within an individual, judgements about illness severity, influences of family history and expectations of an individual’s health trajectory, not just their current health (Idler & Benyamini, 1997; Jylhä, 2009). Although this construct is based on perception and may be driven by mood, when measured using a single item (i.e. how good is your health? (Excellent, good, fair or poor)), poor self-rated health consistently predicted mortality and there was a dose response relationship between increased mortality and poorer rated health in a review of 27 studies using community samples (Idler & Benyamini, 1997). Self-rated health may also reflect health behaviours, for example, poor perceptions of health may result in non-adherence to screening programmes or treatment (Idler & Benyamini, 1997). It was hypothesised that pain would lead to poor self-rated health which in turn would lead to increased mortality through factors associated with poor ratings of health (e.g. illnesses, symptoms).

Functional limitation

The International Classification of Functioning, Disability and Health (ICF) identify three levels of human functioning; 1) body, 2) individual and 3) societal level. Disability is abnormal function at any of the three levels which are known as impairments, activity limitations or participation restriction respectively (World Health Organization, 2002). This section is focussed on limitation at the individual level (i.e. physical limitation which is when an individual has limited capacity to do simple physical tasks for example walk, go up and down stairs and pick up objects (World Health Organization, 2002)). Function within a social context is considered under the category of social factors.

Pain predicts functional limitation (Neogi, 2013). There is a dose-response relationship between increasing low back pain and increasing functional difficulty (Weiner, Haggerty, & Kritchevsky, 2003) and people reporting being often troubled with pain of moderate or severe intensity demonstrated higher rates of functional limitation than those without pain (Covinsky, Lindquist, Dunlop, & Yelin, 2009). Pain (and conditions that pain is the main symptom of) accounts for 5 out of the 10 conditions responsible for the most years lived with disability (YLD) globally with low back pain accounting for 10.7% of all YLD (Buchbinder et al., 2013). Limitations in the ability to perform activities necessary for independent living and self-care are often used as indicators of disability (Chan, Kasper, Brandt, & Pezzin, 2012). Increased functional impairment measured in this way was predictive of mortality in men and women over 65 over a 5 year period (Scott & Macera, 1997) in adult Finnish population (aged 30-91 years, 72% female) over a 5 year period (Sokka & Pincus, 2011) and in an Italian population of adults aged over 80 years (Cesari et al., 2008). A systematic review of studies using objective measures of physical capability

(e.g. walking speed, chair rises) reported low levels of such measures were consistent predictors of all-cause mortality in older community dwelling adults (Cooper, Kuh, Hardy, & Mortality Review Group, 2010). It was therefore hypothesised pain would lead to mortality via functional limitation.

Allostatic load

Allostasis is defined as the physiological adaptation of neural, cardiovascular, neuroendocrine and immune system mechanisms to maintain stability in response to stress (McEwen, 1998). Allostatic load, a dysregulation of these mechanisms, occurs as a result of heightened stress, maladaptation to repeated stressful stimuli and a failure to terminate or regulate competing allostatic system responses (McEwen, 1998).

Allostasis is vital to homeostasis which if not sustained results in mortality (Chapman, Tuckett, & Song, 2008). High allostatic load is associated with cardiovascular disease and cognitive decline (McEwen, 1998) and with frailty (Gruenewald, Seeman, Karlamangla, & Sarkisian, 2009; Szanton, Allen, Seplaki, Bandeen-Roche, & Fried, 2009). Physiological responses to stress in the form of the release of adrenalin, glucocorticoids and cytokines can be damaging if prolonged and can lead to tissue damage and desensitization of receptors (McEwen, 2003).

Pain is a stressor and can lead to the accumulation of allostatic load (Robinson, Edwards, & Iyengar, 2009). Both over-activity and underactivity of the hypothalamic pituitary adrenal (HPA) axis results in allostatic load (McEwen & Seeman, 1999) and abnormalities in the HPA axis have been observed in fibromyalgia patients and low back pain patients (Holliday et al., 2009). Growth hormone deficiencies, specifically low levels of insulin-like growth factor 1 (IGF-1) evident in fibromyalgia patients are also associated with chronic

psychosocial stress (Gupta & Silman, 2004). Chronic pain and high levels of stress in older adults are associated with shorter telomeres than in those without chronic pain and low stress and telomere length is a marker for cellular aging (Sibille, Witek-Janusek, Mathews, & Fillingim, 2012). Shorter telomere length has been shown to be associated with pain in female fibromyalgia patients with those exhibiting higher levels of pain having shorter telomeres than those with lower levels of pain (Hassett et al., 2012). Age related diseases, chronic mental and physical conditions and mortality are also associated with short telomere length, whereas greater telomere length is associated with years of healthy life (Sibille et al., 2012). It was therefore hypothesised that pain would lead to an increase in allostatic load and subsequent mortality.

Frailty

Phenotypic frailty is a geriatric syndrome characterised by declining function across a number of physiological systems (Fried et al., 2001). Fried et al., (2001) developed a 'clinical phenotype' of frailty using participants from the Cardiovascular Health Study of men and women over 65 years from four communities in the United States. Frailty was defined as the presence of three or more of the following characteristics:

- Shrinking – unintentional weight loss of less than or equal to 10 pounds in the previous year
- Weakness – according to grip strength (in the lowest 20% according to sex and BMI)
- Poor endurance and energy – measured via self-report
- Slowness – according to walking speed over a distance of 15 feet (slowest 20% according to sex and height)

- Low physical activity level – measured via self-report (males less than 383Kcals/week, females less than 270 Kcals per week)

(Fried et al., 2001)

Frailty is associated with pain and mortality. In the Cardiovascular Health Study 7% of the cohort met the criteria for frailty which was associated with an increased risk of falls, disability, hospitalisation and mortality (Fried et al., 2001). Shega and colleagues (2012) operationalised frailty in a different way to the phenotype proposed by Fried; 33 self-reported variables pertaining to health attitudes, illnesses (e.g. heart or circulatory problems) functional abilities (e.g. help to take a bath), and living alone were used to generate a composite index from which tertiles representing not frail, pre-frail and frail were derived. They found that frailty status was significantly associated with the report of pain. Participants with moderate or severe pain were over five times more likely to be frail than those without pain (Shega, Andrew, Lau, Weiner, & Dale, 2012). Although this was a cross sectional analysis, the authors suggest pain leads to frailty as a result of reduced physiologic reserve through impaired mobility, depression, decreased nutritional intake, and an increase in the burden of comorbidities (Shega et al., 2012). Convergent validity between the clinical phenotype of frailty and the accumulation of deficits definition has been demonstrated (r=0.65) (Rockwood, Andrew, & Mitnitski, 2007). It was hypothesised that people with pain would be more likely to become frail which would lead to a subsequent increased risk of mortality.

2.8.3 Social factors

Living with pain has a detrimental effect on relationships, interactions with others and on the families of the person with pain (Breivik et al., 2013; Henschke et al., 2015). Social

participation involves interaction with other people in society or the community (Levasseur, Richard, Gauvin, & Raymond, 2010). Participation restriction; difficulties with life situations such as working or shopping, is a negative social consequence of pain (Wilkie, Peat, Thomas, & Croft, 2007). One in five people with chronic pain in Europe reported having lost their job because of pain and one third reported the amount of work they could do or whether they could work at all was affected by their pain (Breivik et al., 2006).

Pain related interference is associated with a reduction in social networks (Peat, Thomas, Handy, & Croft, 2004) and is also associated with neighbourhood deprivation and perceived income inadequacy (Jordan et al., 2008) which may reduce the ability and willingness to undertake social activities. Individuals with chronic pain report difficulty in attending social or family events and participating in recreational activities (Moulin et al., 2002).

Social participation

Participation restriction forms part of the ICF's definition of disability and refers to problems an individual has with involvement in life situations (World Health Organization, 2002). Most definitions of social participation focus on an individual's involvement in activities which involve interaction with others in society or the community (Levasseur et al., 2010). Social participation can help to protect against morbidity and mortality by promoting social interaction which positively influences the sympathetic nervous system and hormone levels such as cortisol which in turn affect blood pressure and the immune system (Holmes & Joseph, 2011). Social participation and social functioning is reduced in people with chronic pain. In a study of chronic pain in Canada by Moulin et al., (2002),

49% of individuals with chronic pain reported experiencing great difficulty in attending social or family events, 61% were unable to participate in their usual recreational activities and 58% could not carry out their usual activities at home (Moulin et al., 2002).

Volunteer work is a form of social participation which provides essential services focussed on creating a better community environment (Jenkinson et al., 2013). It is an important productive activity in older adults and has been shown to be a predictor of reduced mortality (Harris & Thoresen, 2005; Musick, Herzog, & House, 1999) and psychological well-being (Greenfield & Marks, 2004). Pain and related functional limitations were predictors of restriction in paid or voluntary work in 50-59 year olds in North Staffordshire (Wilkie, Blagojevic-Bucknall, Jordan, & Pransky, 2013).

Social and productive activities like volunteering have been shown to confer equivalent survival advantages to fitness activities (Glass, de Leon, Marottoli, & Berkman, 1999). The protective effect of volunteering is greatest in older adults with lower levels of informal social contact and in those who volunteer in moderate amounts but is less protective at higher levels where the detriments associated with role strain may offset any benefits (Musick et al., 1999). Proposed mechanisms linking volunteering to improved well-being include increased opportunity for social contacts and access to resources such as emotional, cognitive or material support and access to health related information (Luoh & Herzog, 2002). It was hypothesised pain would lead to social participation restriction and this would in turn lead to an increased risk of mortality.

2.8.4 Psychological factors

People with persistent pain are more likely to have anxiety or depressive disorders than those without pain (Gureje & Korff, 1998; Robinson et al., 2009). Suicidal ideation is three

times more common in people with chronic pain compared to those without chronic pain (Tang & Crane, 2006). The psychological processes of helplessness and hopelessness about pain, the desire for escape from pain, catastrophizing, avoidance and problem solving deficits have been highlighted as important to understanding this suicidality (Tang & Crane, 2006). Cognitive function is also reduced in individuals with pain (Moriarty, McGuire, & Finn, 2011).

Quality of life (QoL) and wellbeing are subjective perceptions which overlap with and interlink individual consequences of pain. They are closely related concepts and many definitions of each concept exist. The World Health Organisation define QoL as "an individual's perception of their position in life, in the context of the culture and value systems in which they live, and in relation to their goals, standards and concerns. QoL is a broad ranging concept, affected in a complex way by the person's physical health, psychological state, level of independence, social relationships and their relationship to salient features of their environment" (WHOQOL Group, 1995). A more recent definition of wellbeing describes the concept as "an umbrella term for different valuations people make regarding their lives, the events happening to them, their bodies and minds and the circumstances in which they live" (Diener, 2006). Both of these definitions take into account life circumstances and values and reflect subjective rather than objective measures (Camfield & Skevington, 2008). Ratings of QoL and wellbeing are influenced by the presence, combination and relative importance of different factors to the individual. As already outlined, reductions in a number of indicators of wellbeing are evident in individuals with pain and they do not act in isolation. For example physical performance and disability levels are strongly associated with pain-related fear in patients with

musculoskeletal pain syndromes like fibromyalgia. This can result in fear avoidance and depression, reducing daily function and quality of life for those people. These factors along with fatigue and sleep disturbance which are also consequences of pain may in turn result in a reduction of leisure time activity and social contact (Tüzün, 2007). Understanding such processes is important for our understanding of the impact of pain.

Quality of life

Historically, measures of health such as activities of daily living have been used as indicators of quality of life in older people (Hyde, Wiggins, Higgs, & Blane, 2003) but it is recognised as being a complex multidimensional concept with includes both objective and subjective aspects (Van Malderen, Mets, & Gorus, 2013). Indicators of quality of life such as physical functioning, mental health and emotional and social well-being are reduced in people with pain (Ang et al., 2006; Niv & Kreitler, 2001; Tüzün, 2007) and lower scores for health related quality of life (HRQOL) are associated with a higher risk of mortality (Kaplan et al., 2007; Mapes et al., 2003). Hearing, mobility and pain are specific components of health related quality of life (HRQoL) that are predictive of mortality (Feeny et al., 2012). It was hypothesised pain would lead to reduced quality of life and this would predict a subsequent increased risk of mortality.

Anxiety and Depression

The World Health Organisation define depression as "a common mental disorder, characterised by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness and poor concentration" (WHO, 2015c). Anxiety is a broad term used to describe a number of different disorders but general anxiety is often characterised by worrying thoughts, feelings of being tense and

frightened, restlessness and panic (Mykletun et al., 2009). Symptoms of depression and anxiety often co-occur with chronic pain in primary care. Patients with a combination of pain and depression or pain and anxiety report greater severity of pain than those with pain alone, and those with both anxiety and depression report the most severe pain (Bair & Wu, 2008).

The prevalence of depression is greater in people with pain than in individuals without pain (Bair & Robinson, 2003; Robinson et al., 2009). The relationship between pain and depression is reciprocal. Pain at baseline was an independent predictor of becoming depressed two years later, and depression at baseline predicted pain two years later in a study conducted using participants from the English Longitudinal Study of Aging (ELSA) (Chou, 2007).

The presence of pain can be a barrier to the recognition and treatment of depression (Bair & Robinson, 2003) however, the conditions of pain and depression have been shown to share biological pathways and neurotransmitters and respond to similar treatment (Dunne, 2011). Activation of the HPA axis and the ascending and descending pain tracks are common to both conditions (Robinson et al., 2009).

Anxiety and depression are also associated with mortality (Mykletun et al., 2009). Increased mortality rates have been observed in both clinically and sub-clinically depressed individuals (Mykletun et al., 2009). Proposed mechanisms include suicide, increased hazardous health behaviours, higher rates of accidental deaths, and adverse effects of depression on endocrine, neurologic and endocrine processes, interference with a patient's motivation for recovery and by affecting compliance with treatment (Cuijpers & Smit, 2002).

Studies by Dreyer et al., (2010) and Wolfe et al., (2011) reported a significantly increased risk of death from suicide in patients with fibromyalgia (Dreyer et al., 2010) (Wolfe, Hassett, Walitt, & Michaud, 2011). Many of the risk factors for suicide are also associated with chronic pain such as depression and histories of drug and alcohol abuse (Cheatle, 2011). Often opioids are prescribed for pain problems thus providing a potentially lethal medication to vulnerable people (Cheatle, 2011). An increase in the number of deaths due to poisoning with opioid analgesics has been observed in the United States between 1999 and 2006 (Warner, Chen, & Makuc, 2009).

In a review of literature examining suicidality in chronic pain Tang and Crane (2006) found double the risk of suicide in patients with chronic pain relative to controls. They identified a number of risk factors associated with suicidality in chronic pain. These include type, intensity and duration of pain, insomnia, helplessness and hopelessness about pain, the desire for the escape from pain, pain catastrophising and avoidance and problem solving deficits (Tang & Crane, 2006).

Conversely, positive psychological wellbeing is associated with reduced mortality in both healthy populations and in those with existing physical illness (Chida & Steptoe, 2008, Keyes & Simoes, 2012). Anxiety and depression were therefore hypothesised to be intervening factors on pathways between pain and mortality.

Cognitive impairment

Cognitive function refers to attention, learning and memory, speed of information processing, psychomotor and executive function (Moriarty et al., 2011). Cognitive impairment is common people with pain. It is an important determinant of independence

in older adults and therefore an important component of healthy ageing (Llewellyn, Lang, Langa, & Huppert, 2008). In a review of clinical and preclinical studies Moriarty et al., (2011) concluded that pain was associated with impaired attentional, executive and general cognitive functioning. They proposed the mechanisms were a result of pain competing with limited cognitive resources, neuroplasticity and dysregulated neurochemistry (Moriarty et al., 2011). Severe and mild cognitive impairment and poor memory performance is also associated with an increased risk of mortality (Bassuk, Wypij, & Berkman, 2000; Shipley, Der, Taylor, & Deary, 1985). Cognitive impairment has been shown to be associated with the presence of inflammatory markers and haemostasis (Rafnsson et al., 2007) or may be a side effect of analgesic medication (Moriarty et al., 2011) which may in turn lead to an increased risk of mortality. Cognitive decline is also associated with physical decline, an increased likelihood of being placed in a nursing home and subsequent increased mortality (Wolinsky et al., 2006). Cognitive impairment was therefore hypothesised to provide a link between pain and mortality.

Perceived control over health

The way an individual perceives their illness or condition can affect the way they respond to it. Leventhal and colleagues proposed a parallel-processing model of illness representation and coping mechanisms known as the Self-Regulatory Model (SRM) (Leventhal, Diefenbach & Leventhal, 1992). This incorporates cognitive and emotional aspects of illness perception and behaviour and posits a framework, which can be used to help understand people's reaction to illnesses and their treatment. The SRM suggests that health related behaviour such as adherence to medical treatment is strongly influenced by an individual's representation of the illness threat. Five dimensions of illness representation are incorporated into the model. These are:

- Identity (what is it? – the name or label given to the conditions and its symptoms)
- Time-line (how long will it last? Will it be acute or chronic?)
- Cause (what is perceived to have caused the illness?)
- Consequences (how will it affect the individual?)
- Control/cure (can it be controlled or cured and what role does the individual play in this?)

Patient perceptions are an important determinant of future clinical outcomes. Good clinical outcomes in low back pain patients were observed for those who perceived less serious consequences, reported fewer emotional responses, attributed fewer symptoms to their condition and had stronger perceptions regarding their ability to control their pain (Foster et al., 2008). Negative illness perceptions were associated with an increased risk of mortality in end stage renal disease patients, and in particular their beliefs about treatment control (Parfeni, Nistor, & Covic, 2013) and low perceived control explained much of the link (51%) between low socioeconomic status and mortality in a study of Dutch adults aged 25-74 years over a six year follow up (Bosma et al., 1999). Low perceived control over health as a result of pain was hypothesised to lead to subsequent mortality.

2.9 Potential moderators of a relationship between pain and mortality

The proposed pathways between pain and mortality described above may be different in different sub-groups of the population. This can be tested using moderation analysis. Sex and the presence of comorbidity were proposed as moderating factors in this thesis.

2.9.1 Sex

Pain experience is different in men and women and a clearer understanding of why this occurs can inform the management of pain (Greenspan et al., 2007). As described in Section 1.5.3, the prevalence of pain is greater in females and is due to biological (e.g. hormonal modulation) and psychosocial factors (e.g. catastrophizing and use of coping strategies) (Fillingim et al., 2009; Wijnhoven et al., 2006). The impact of pain is often greater in women (Henschke et al., 2015; Reyes-Gibby et al., 2002; Smith et al., 2001) and disabling back pain has been linked to an increased risk of mortality in women but not men (Docking et al., 2014) suggesting there may be sex differences in pathways from pain to mortality. Women are more likely to experience anxiety and depression, physical and somatic conditions and disability related to their pain than men (Greenspan et al., 2007). Women with pain are more likely to catastrophise than men but are also more likely to seek social support and use more coping strategies than men (Fillingim et al., 2009). Keefe et al., (2000) found that catastrophising mediated gender differences in osteoarthritis (OA) pain-related outcomes (pain intensity, pain behaviour, physical disability) even after controlling for depression (Keefe et al., 2000). Pain is associated with the negative effects of alcohol consumption (physical or psychological problems or social conflicts) in men but not women (Brennan et al., 2011). Sleep problems (which are associated with pain (see section 2.8.1)) are associated with greater psychological distress, higher fasting insulin, fibrinogen, and inflammatory biomarkers (markers for allostatic load) (Suarez, 2008) and hypertension (Cappuccio et al., 2007) in women but not men. Other factors associated with pain demonstrate differences between men and

women and could influence differences in mortality risk, for example there are stronger associations between social participation and survival in women compared to men (Agahi & Parker, 2008). In a systematic review of physical activity in non-institutional adults over 60 years, women were less likely to achieve regular physical activity (measured by both subjective and objective measurements) compared to men (Sun, Norman, & While, 2013). Women are more susceptible to smoking related diseases than men irrespective of differences in smoking behaviour (Peters, Huxley, & Woodward, 2014) and globally, more women than men are obese (10% of men cf 14% of women in 2008) (WHO, 2015c). These differences in factors related to pain indicate there may be different indirect pathways from pain to mortality in men compared to women.

2.9.2 Comorbidity

Chronic widespread pain often occurs alongside other symptom based conditions such as chronic fatigue syndrome, irritable bowel syndrome and psychiatric disorders such as anxiety and depression (Kato & Sullivan, 2006). However, the presence of chronic physical conditions is not always accompanied by the report of pain providing support for the recognition of chronic pain as an individual condition (Dominick et al., 2012). The presence of comorbidity increases the burden of illness and is likely to affect treatment outcomes (Greenspan et al., 2007). Studying comorbidity is complex due to the many different combinations of medical conditions that co-exist that may require similar or distinct treatment strategies, however additional morbidity is associated with decreased quality of life, psychological distress, longer hospital stays, more post-operative complications, higher costs of care and higher mortality (Fortin, Soubhi, Hudon, Bayliss, & van den Akker, 2007; Valderas & Starfield, 2009). It was therefore hypothesised the risk

of mortality for people with pain would be greater in those who also reported other medical conditions (referred to as comorbidity). This indicates there may be differences in the strength and nature of the pathways from pain to mortality between those with and those without comorbidity.

This thesis will now go on to describe an examination of the influence of pain phenotype on the relationship between pain and mortality and an investigation of the role of potential mediators and moderators of the relationship (described in this section). The specific aims and objectives are presented in Chapter Three.

2.10 Key messages

- A modest but non-significant relationship between chronic pain and mortality was indicated in the systematic review, particularly cancer mortality.
- Harmonised data collection, consistent pain phenotypes, sample populations and methods of analyses which result in comparable outcome measures (e.g. MRR or SMR) are required to robustly determine whether chronic pain increases the risk of mortality.
- An investigation of the role of lifestyle, health, social and psychological factors is warranted to provide a clearer understanding of the relationship between chronic pain and mortality.

Chapter Three. Aims and objectives

3.1 Aims

The aims of the analyses presented in this thesis were to gain a better understanding of the link between pain and mortality by investigating the role of pain phenotype and to investigate potential mechanisms for a relationship between pain and mortality.

3.2 Specific objectives

The specific objectives addressed in this thesis were to:

1. Assimilate existing evidence for a relationship between chronic pain and mortality through a systematic review and meta-analysis.
2. Determine:
    a) Which pain phenotypes are associated with mortality (all-cause and cause specific)?
    b) Whether the relationship between pain and mortality is mediated by lifestyle factors (e.g. physical inactivity), health factors (e.g. poor self-rated health), social factors (e.g. low social group membership) and psychological factors (e.g. depression).
    c) Whether the relationship between pain and mortality is moderated by sex and health status (e.g. comorbidity).

3.3 Thesis content

The following section gives a broad overview of the content in each subsequent thesis chapter.

Chapter Four. Data sources

The empirical analyses in this study used data collected in the English Longitudinal Study of Ageing (ELSA) and the North Staffordshire Osteoarthritis Project (NorStOP). This chapter provides a critical overview of the ELSA and the NorStOP methods including sampling techniques and data collection. It describes the stages of the assessment of the suitability of the data to address the objectives of this thesis; this includes evaluation of response rates, missing data and power of the data samples to detect a relationship between pain and mortality. It also includes evaluation of the internal and external validity of results.

Chapter Five. The influence of pain phenotype on mortality

This chapter presents the analysis of the associations between pain phenotype and mortality in adults aged 50 years and over. It describes survival analysis of the association between mortality and the following pain phenotypes:

- “often troubled” with pain and pain intensity using ELSA data
- “any pain”, widespread pain (ACR criteria, Manchester criteria), number of pain sites and pain interference using NorStOP data.

Chapter Six. Mechanisms of association between pain and mortality

This chapter presents the analyses investigating mediation and moderation of the relationship between pain and mortality.

Chapter Seven. Discussion and conclusions

This chapter presents a brief overall summary of the thesis and a critical re-examination of the findings. Based on this, the implications for future research and ways to reduce the impact of pain are discussed.

Chapter Four. Data sources

4.1 Introduction

Chapter Two described a systematic review of studies which had examined the relationship between chronic pain and mortality. Differences in the study populations, pain phenotypes and confounders may explain the inconsistencies in results. Further investigation of the role of pain phenotype and the identification of mediating and moderating factors of this relationship would enhance the understanding of the relationship between pain and mortality. Large population studies, in which there has been extensive data collection, provide the opportunity to examine different pain phenotypes and a number of mediators and moderators.

This chapter describes two population based cohort studies from which data was used to fulfil the objectives outlined in Chapter Three; the English Longitudinal Study of Ageing (ELSA) and the North Staffordshire Osteoarthritis Project (NorStOP). ELSA was used in this study as it was designed to be nationally representative which reduces the likelihood of sampling bias and it collected data on a number of lifestyle, health, social and psychological factors which could be included in the analyses as potential moderators and mediators. NorStOP was designed to study the prevalence and impact of pain in a community sample of adults aged 50 years and over. NorStOP contained detailed information on pain which allowed a more comprehensive investigation of the effect of pain phenotype on the relationship between pain and mortality and further added to the ELSA analyses by providing the opportunity to investigate additional mediators not examined in the ELSA sample. Additionally, as ELSA and NorStOP are longitudinal studies, this provided scope to measure change over time of mediating factors. Both datasets

were studies of older adults and the samples derived from them for the current study included adults aged over 50 years only. As detailed in Chapter One, the prevalence and impact of pain is greater in older age groups, therefore if a relationship between pain and mortality exists it may be stronger in this age group and there would be greater scope for examining potential mechanisms as a result of the impacts of pain on life reported by older adults.

This chapter presents an overview of data collection methods, sampling techniques and the response rates for each dataset. An examination of missing data and power analyses were undertaken to determine potential sources of bias and whether the achieved samples were of sufficient size to detect the expected effects. More detail regarding the measurement of individual variables is provided in Chapters Five and Six.

4.2 Aims

The aim of this chapter was to evaluate the capacity of the ELSA and NorStOP datasets to achieve the objectives of this thesis. The objectives of the investigations undertaken in this chapter were to:

1) Identify the extent of non-response and potential for selection bias in the samples used in the analyses.
2) Determine if the derived samples had sufficient power to detect the estimated effect size of a relationship between pain and mortality.
3) Assess whether the derived samples were representative of the larger national (England and Wales) population.

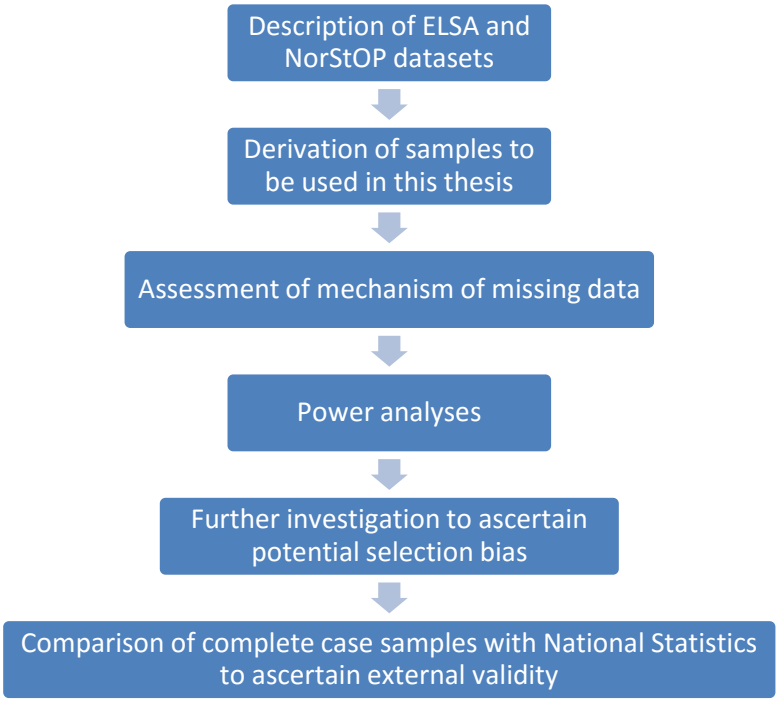


Figure 4.1 Flow diagram of Chapter Four

4.3 Preparation and analysis of datasets

The author of this thesis (i) planned the analysis, (ii) requested and acquired the data from ELSA and NorStOP and (iii) completed the analysis.

Data from ELSA were downloaded from the UK Data Service website following registration with the UK data service (i.e. at https://discover.ukdataservice.ac.uk/series/?sn=200011#access). The data were available in multiple datasets (for example from different time points and data collected via nurse visit) which were then merged by the candidate. The raw data was recoded as variables for this analysis.

NorStOP data were acquired from the Research Institute for Primary Care and Health Sciences at Keele University following an in-house data request. As with ELSA, some

variables were recoded and datasets were merged. Further details of both datasets are presented in the current chapter. Details of the recoding of individual variables for both datasets are available in Appendix VII. All preparation and subsequent analysis (detailed in the current Chapter and Chapters Five and Six) was carried out by the candidate. The R code used in Chapter Six to undertake the mediation analysis within survival anlaysis was prepared by a statistician (Milica Blagojevic-Bucknall) but all models were run by the candidate. Separate datasets were created for each mediation model containing just predictor, outcome, confounder and individual mediator data (detailed in Chapter Six) in order to reduce the amount of time taken to run the models.

4.4 Study design

4.4.1 The English Longitudinal Study of Ageing (ELSA)

The English Longitudinal Study of Ageing (ELSA) is a nationally representative population based study of older adults. The primary objective of ELSA is to collect longitudinal data from a representative sample of the English population aged 50 years and older (Scholes, Taylor, Cheshire, Cox, & Lessof, 2008).

ELSA is a large scale longitudinal panel study meaning repeated measures are taken at regular time intervals (in this case every two years) of the health, economic and social circumstances of adults aged 50 years and over drawn from a sample of private households that had previously responded to the Health Surveys for England (HSE) in 1998, 1999 and 2001. ELSA was developed through collaboration between University College London, the Institute of Fiscal Studies and the National Centre for Social Research (NatCen). Funding for the study was provided by the US National Institute on Aging and a

consortium of British Government Departments. Ethical approval for ELSA was granted from the London Multicentre Research and Ethics Committee and informed consent was obtained from all participants. This was obtained through the use of consent forms where participants were asked for their permission to be re-contacted at future waves and give consent for their survey data to be linked to National Insurance records, welfare and benefit information, tax credits, mortality and cancer registration and hospital episode statistics (HES) (Scholes et al., 2008).

The HSE was designed to be nationally representative of private households. It used the Postcode Address File (PAF) to identify eligible households. The PAF is the most comprehensive and up-to-date database of UK addresses and postcodes and contains 29 million business and residential addresses (to which mail can be delivered) and 1.8 million postcodes (Royal Mail Ltd, 2015). The HSE ensured every residential address in this file had an equal chance of inclusion by using a random probability sample of households. The HSE is a series of surveys with a new sample each year. The HSE years 1998, 1999 and 2001 were selected as a sampling frame for Wave 1 of ELSA. These were the most recent surveys at that time and produced a sufficiently large sample size (23,132 households). (The 2000 survey focussed on adults over 65 so was not used in the sampling frame for ELSA) (NatCen Social Research, 2014a).

The first Wave of ELSA took place in 2002 and data was subsequently collected at two-yearly intervals. Participants were eligible for interview if they were born before 1st March 1952 and were living at a private residential address. Refreshment samples were used at Waves 3, 4 and most recently Wave 6 in order to maintain representation of those in

their early 50s. These were people sampled from the HSE from 2001 to 2006 who were previously too young to take part in ELSA (Banks et al., 2014).

Method of administration

Information for the main survey was gathered using a personal face to face interview using computer aided personal interviewing (CAPI) and a self-completion questionnaire. All interviewers underwent a two-day briefing by a researcher prior to undertaking the interview which included how to administer the assessments, an explanation of all documents needed and an introduction to the questions for the CAPI interview (Taylor et al., 2007). Information was collected about household and individual demographics, physical and psychosocial health, work and pensions, income and assets, housing, cognitive function, social participation and expectations for the future at each wave. As a check, one-in-ten participants were contacted by telephone to verify key details from their interview (Taylor et al., 2007). A separate nurse visit was included at Waves 2 and 4 to collect blood samples and anthropometric and physical measurements. Appointments for the nurse visits were made at the time of interview and were only carried out once the appropriate consents were obtained. Seven consent forms were presented in a booklet which participants were asked to sign allowing blood to be taken, consenting for information on blood pressure, lung function, and blood results to be sent to their GP, allowing storage of their blood for future use, for extraction and storage of DNA and for saliva to be tested for cortisol for use in future research (Scholes et al., 2008).

Data on potential mediators were collected at multiple waves of ELSA. This offered the potential to construct variables which identified change over time in mediating constructs (i.e. this would allow modelling of whether the relationship between pain and mortality

was mediated by change in potential mediators). The current study used information collected at Wave 2, defined here as “baseline” and Wave 4, defined here as “follow-up” in order to use biomarker information to generate allostatic load and frailty variables; these are proposed mediators, and their methods of measurement are described in Section 6.3.3. Fieldwork for Wave 2 took place between June 2004 and July 2005. For Wave 4 data was collected between May 2008 and July 2009 (NatCen Social Research, 2014b).

Response to the survey was encouraged by an offer of a £10 gift voucher to be provided at the end of the interview. Responders were assigned the same interviewer at subsequent waves where possible and where members of households were no longer living together attempts to contact responders at both old and new addresses were made to try and ensure all those eligible had the opportunity to take part. If an individual was unable to take part as a result of cognitive impairment or illness a proxy interview was attempted with an informant. This was usually a family member but was anyone over the age of 16 who could provide the relevant information about the individual (Scholes et al., 2008). If the self-completion questionnaire was not returned a reminder was sent and if this was also unsuccessful a member of the NatCen Telephone unit would call the respondent and complete the form on their behalf from their answers provided via telephone (Scholes et al., 2008).

Data processing

The coding of closed questions was undertaken through the code frame within the CAPI system. Responses to ‘open’ questions were coded into separate variables after the interview using a separately developed code frame where a few new answer codes were

generated where answers did not fit existing codes. Coding and editing was undertaken by the interviewers in the field with some post interview checks where inconsistencies arose. All ELSA data files deposited in the archived dataset were given a unique individual serial number to enable users to link different files. Data dropped from the archived dataset included the name and address of the respondent and variables such as detailed ethnicity, specific country of birth, full interview data and full date of birth to reduce the potential of identifying individuals who took part (NatCen Social Research, 2014b).

Table 4.1 presents the variables obtained from ELSA and their proposed role in this study of the relationship between pain and mortality. Details of how each variable was measured are presented in Chapters Five and Six.

Table 4.1 The role of ELSA variables in the survival analysis (Chapter Five) and the mediation and moderation analyses (Chapter Six)

Concept	Predictor	Outcome	Moderator	Mediator	Confounder
Pain	X				
Mortality		X			
DEMOGRAPHICS					
• **Age**					X
• **Sex**			X		X
• ***Education***					X
• ***Wealth***					X
LIFESTYLE FACTORS					
• ***Physical activity***				X	
• ***Smoking***				X	
• ***Alcohol consumption***				X	
HEALTH					
• ***Self-reported health***				X	
• ***Functional limitation***				X	
• ***Comorbidity***			X		
• ***Allostatic load***				X	
• ***Frailty***				X	
SOCIAL FACTORS					
• ***Volunteer work***				X	
• ***Social group membership***				X	
PSYCHOLOGICAL FACTORS					
• ***Quality of Life***				X	
• ***Depression***				X	
• ***Cognitive impairment***				X	

4.4.2 The North Staffordshire Osteoarthritis Project (NorStOP)

The NorStOP is a population based cohort study designed to assess the prevalence and impact of pain in a community sample of adults aged 50 years and over. Data from three cohorts of NorStOP (i.e. NorStOP 1, NorStOP 2 and NorStOP 3) were used in this study. These were designed as population cohort studies and collected similar data at baseline, three and six year follow-ups. The aim of NorStOP 1, 2 and 3 was to examine the natural history of joint pain in the general population. NorStOP 2 and 3 additionally aimed to identify older adults with knee and hand pain respectively, for clinical studies. For the current study, data collected at baseline and three year follow-up were used. Baseline data for each cohort was collected at different time points (i.e. NorStOP 1 was collected in April 2002, NorStOP 2 was collected from July/August 2002 to July/August 2003 and NorStOP 3 was collected from March 2004 to April 2005). Ethical approval for NorStOP was granted from the North Staffordshire Local Research Ethics Committee (REC reference numbers 1351, 1430 and 05/Q2604/20) (Thomas, et al., 2004).

Eight practices from the North Staffordshire General Practice Research Network were recruited to the study; three for NorStOP 1, three for NorStOP 2 and two for NorStOP 3. In 2001 (when NorStOP was developed) North Staffordshire consisted of four Primary Care Trusts. It had a combined population of approximately 460,000 (Office For National Statistics, 2001). The eight practices were located in urban and rural areas. There were 101 general practices in North Staffordshire, 16 of which formed the General Practice Research Network. These latter practices continuously collated information regarding clinical contacts to facilitate epidemiological research and have undergone annual audits by Keele's Primary Care Sciences Research Centre Health Informatics team to assess the

quality and completeness of their data. The age-sex registers from the eight practices were used to provide a representative sample of the local general population. 98% of people in the United Kingdom are registered with a general practitioner (Bowling, 2009) and so the registers were a convenient sampling frame for a local population. Overall for the three NorStOP cohorts 26,705 adults were included in the original sampling frame and were sent baseline questionnaires.

Method of administration

A two-stage methodology was used for each cohort at each data collection (baseline and three year follow-up). Prior to each mailing the contact details of all adults aged 50 years and over from each practice list were checked by the GPs from the practices for exclusions. Patients were excluded if they were unable to complete the questionnaire due to illness, were known to have severe learning disabilities or a severe psychological disorder, or had indicated previously that they did not wish to take part in research projects prior to the mailing procedure.

Keele's Primary Care Research Centre has robust data security systems and procedures in place which achieve the legal obligations set by the Data Protection Act and follow General Medical Council (GMC), Caldicott Guardian and British Computer Society standards and guidelines. Personally identifiable data was held only for as long as was needed (e.g. to undertake mailing) and identifiable data was stripped from research databases as soon as was feasible. Each individual in the sample population was allocated a unique study number on all questionnaires and survey data was separated from all contact details so that only anonymised data was available for analysis.

In the first stage, all eligible participants were mailed a “Health Survey” questionnaire. In the second stage, responders to the “Health Survey” questionnaire who gave permission to be re-contacted and who reported experiencing either a hand problem or pain in at least one of four regional sites (hands, hips, knees, or feet) in the previous 12 months were mailed a “Regional Pain Survey” questionnaire, which focused on these four regional sites. The current study used data from the “Health survey” only. At each stage, questionnaires were accompanied by a letter from the GP practice and a study information leaflet. Reminders were sent to non-responders after two weeks (postcard only) and four weeks (a further questionnaire and letter from the GP). Throughout the study, those mailed the questionnaires were offered the opportunity to contact the Research Centre to discuss the study in further detail with the Study Co-ordinators.

Questionnaire processing

On return of the completed questionnaires, the date of birth and sex given by the responders were checked against those from the surgery records to ensure replies were from the intended responder. Questionnaires were then placed in secure storage, for pre-scan checking. Data was entered using an automatic data entry system called Teleform^{TM}, which demonstrates high levels of data accuracy (Jinks, Jordan, & Croft, 2003).

To establish the accuracy of the scanned data, the data was checked for errors. The paper copy of the questionnaire was checked against the exported data in SPSS. The questionnaire identification number was noted on a proforma along with any identified errors. After the scanning of each of the first five boxes one in five questionnaires were checked. After this, data were checked after all data entry had been completed, where

again one in five questionnaires were checked. Identified errors were corrected in the SPSS file.

Manikin data entry

The "Health Survey" questionnaire contained a manikin body chart (Chapter Five, Figure 5.1). Data entered on this could not be processed using the automatic data entry system and was processed manually using a Microsoft Access database. Those mailed the "Health Survey" were asked to shade in areas of the body chart where they had aches or pains that had lasted for one day or longer in the previous four weeks (not including pain occurring due to illness such as flu). The areas of pain were coded manually using three plastic transparent templates to enable a comprehensive assessment using previously published manikin criteria:

(i) Template 1 scored widespread pain and had 42 areas (Macfarlane, Croft, Schollum, & Silman, 1996).

(ii) Template 2 scored neck pain (area 43) (Papageorgiou et al., 1996) and hip pain (areas 44-47) (Birrell et al., 2000).

(iii) Template 3 scored lower back pain (area 48) (Papageorgiou, Croft, Ferry, Jayson, & Silman, 1995).

Manikin data entry was checked by another data clerk, who performed the same procedure and noted errors on a proforma. Identified errors were corrected in the database.

Data cleaning

The data processed in the Teleform™ system was exported to a SPSS file. This file was checked to identify anomalies in the full data set. This was particular to items where responses were hand-written:

(i) Date of birth and sex – where the date of birth was missing, the signature on the questionnaire was checked against the name on the mailing list to ensure that the correct person had returned the questionnaire. The date of birth and sex values were then taken from the mailing list and used in the questionnaire database.

(ii) Height and weight – any unrealistic values were scored as missing, for example heights greater than 8 feet or weights greater than 30 stones.

(iii) Age left school – any unreasonable values were scored as missing, for example ages less than 12 or greater than 25 years.

Details of the proposed role of the NorStOP variables used in this study are presented in Table 4.2. Measurement methods for individual variables are presented in Chapters Five and Six.

Table 4.2 The role of NorStOP variables in the survival analysis (Chapter Five) and mediation and moderation analyses (Chapter Six)					
Concept	**Predictor**	**Outcome**	**Moderator**	**Mediator**	**Confounder**
Pain	X				
Mortality		X			
DEMOGRAPHICS • **Age** • **Sex** • ***Education*** • ***Adequacy of income***			 X		 X X X X
LIFESTYLE FACTORS • ***Smoking*** • ***Alcohol consumption*** • ***Obesity*** • ***Physical activity(walk/go out)*** • ***Sleep***				 X X X X X	
HEALTH • ***Self-rated health*** • ***Functional limitation*** • ***Comorbidities***			 X	 X X	
SOCIAL FACTORS • ***Social Participation***				 X	
PSYCHOLOGICAL FACTORS • ***Anxiety*** • ***Depression*** • ***Cognitive impairment*** • ***Perceived control of health***				 X X X X	

4.5 Participant flow

4.5.1 ELSA

The target sample for ELSA consisted only of households containing at least one living age-eligible individual (aged 50 years and over) who had agreed to be contacted in the future. This resulted in the exclusion of 11,554 households from the original HSE sampling frame (n=23,132) resulting in 11,578 households containing 18,813 age-eligible sample members or younger partners. Data was obtained from 12,100 of these participants by interview. The main reason for non-response to the first wave of ELSA was refusal to take part. Other reasons were language difficulties, illness or absence during the survey period

or physical or mental difficulties preventing individuals from taking part (Taylor et al., 2007).

Table 4.3 displays the age/sex distribution of the target sample (study population) and the responders. This is based on the respondent's age at the time of interview. Responders were defined as individuals who gave a full or partial interview in person or by proxy. However in addition to sample members, younger partners and new partners were also interviewed. The 'responders' sample is therefore not a sub-group of the target population but from observation the age and sex distribution of both groups is similar. However the oldest age group is underrepresented for both men and women compared to the national population (Taylor et al., 2007).

Table 4.3 The anticipated and achieved Wave 1 ELSA sample stratified by age and sex

Age group	Study population n=18,813			Responders n=12,100*		
	Male	**Female**	**Total**	**Male**	**Female**	**Total**
Under 50	220 (3%)	822 (8%)	1042 (6%)	104 (2%)	472 (7%)	576 (5%)
50-59	3224 (38%)	3528 (34%)	6752 (36%)	1930 (36%)	2327 (34%)	4277 (35%)
60-69	2450 (29%)	2556 (25%)	5006 (27%)	1619 (30%)	1795 (26%)	3414 (28%)
70-79	1792 (21%)	2077 (20%)	3869 (21%)	1178 (22%)	1393 (21%)	2571 (21%)
80+	802 (10%)	1329 (13%)	2131 (12%)	485 (9%)	777 (11%)	1262 (10%)
Unknown	9 (0%)	4 (0%)	13 (0%)	-	-	-
Total	8497	10316	18813	5336	6764	12100

* The ELSA Wave 1 technical report (Taylor et al., 2007) was written before the data were fully reconciled and it has subsequently been noted there were some small errors in the original report (e.g. duplicate households, changes to outcome codes). As a result of this the total number of responders at Wave 1 was reduced to 12,099 and is reported as such in later written material (Institute for Fiscal Studies, 2015).

Wave 2 took place in 2004. All responders at Wave 1 were approached and 8781 were retained in Wave 2. Non responders (n=3318) at Wave 2 were more likely to have a long term limiting illness, be of lower socioeconomic status, be non-white, female and aged over 85 at Wave 1 (Scholes et al., 2008). The Wave 2 sample for analysis also included 652 additional participants (core, young and new partners) to provide a total sample of 9432. The reporting of response rates and attrition in ELSA is challenging because there

were variations in the responses to different elements of the study, deaths, differences between core and refreshment cohorts, and some individuals failed to respond at one wave but re-joined the study at later waves (Steptoe, Breeze, Banks, & Nazroo, 2012). People lost to follow-up tended to be older, less wealthy and less educated, come from a non-managerial occupation and suffer from a long standing limited illness (Steptoe et al., 2012). The number of participants who provided complete data at each wave of ELSA is illustrated in Figure 4.2.

As previously stated Wave 2 (2004) of ELSA was used as baseline in this study and Wave 4 (2008) as the follow-up time point to use biomarker information collected during these waves. The two time points were necessary to examine the effect of the change over time of potential mediators of the association between pain and mortality. 9432 interviews took place at Wave 2 and of these participants, 7666 had nurse visits. Reasons for non-completion of the nurse visit included refusal, unable to contact to arrange a visit, being too ill or being away at the time of the planned visit (Scholes et al., 2008).

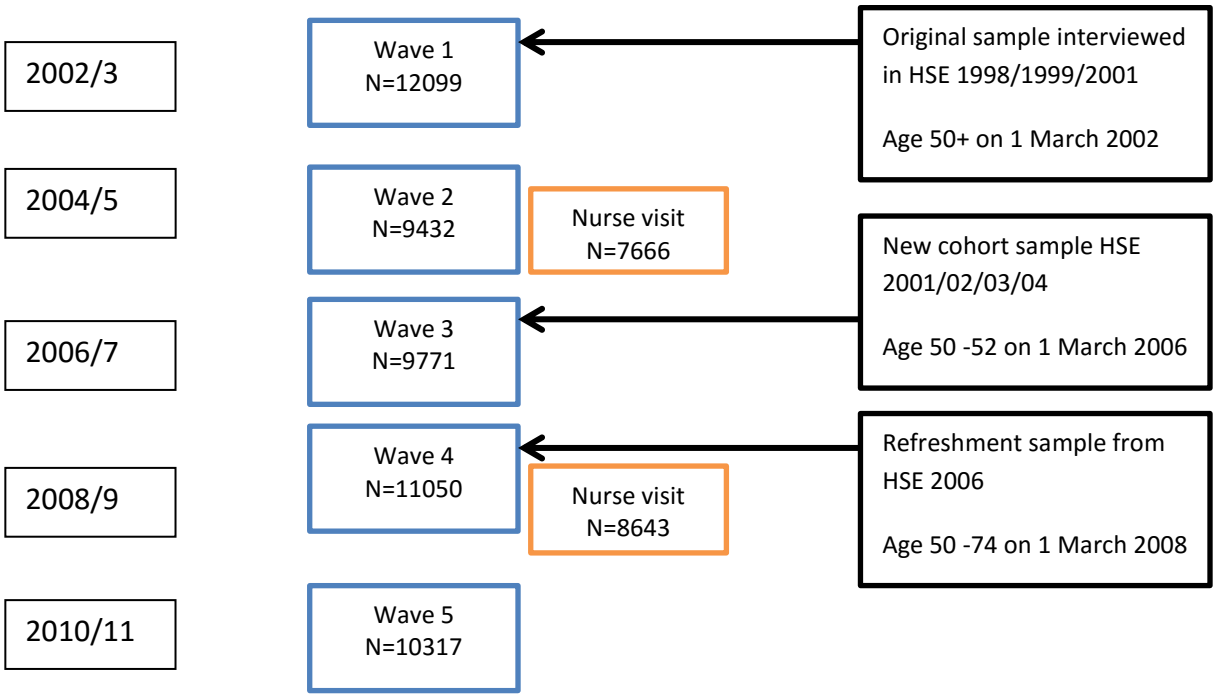
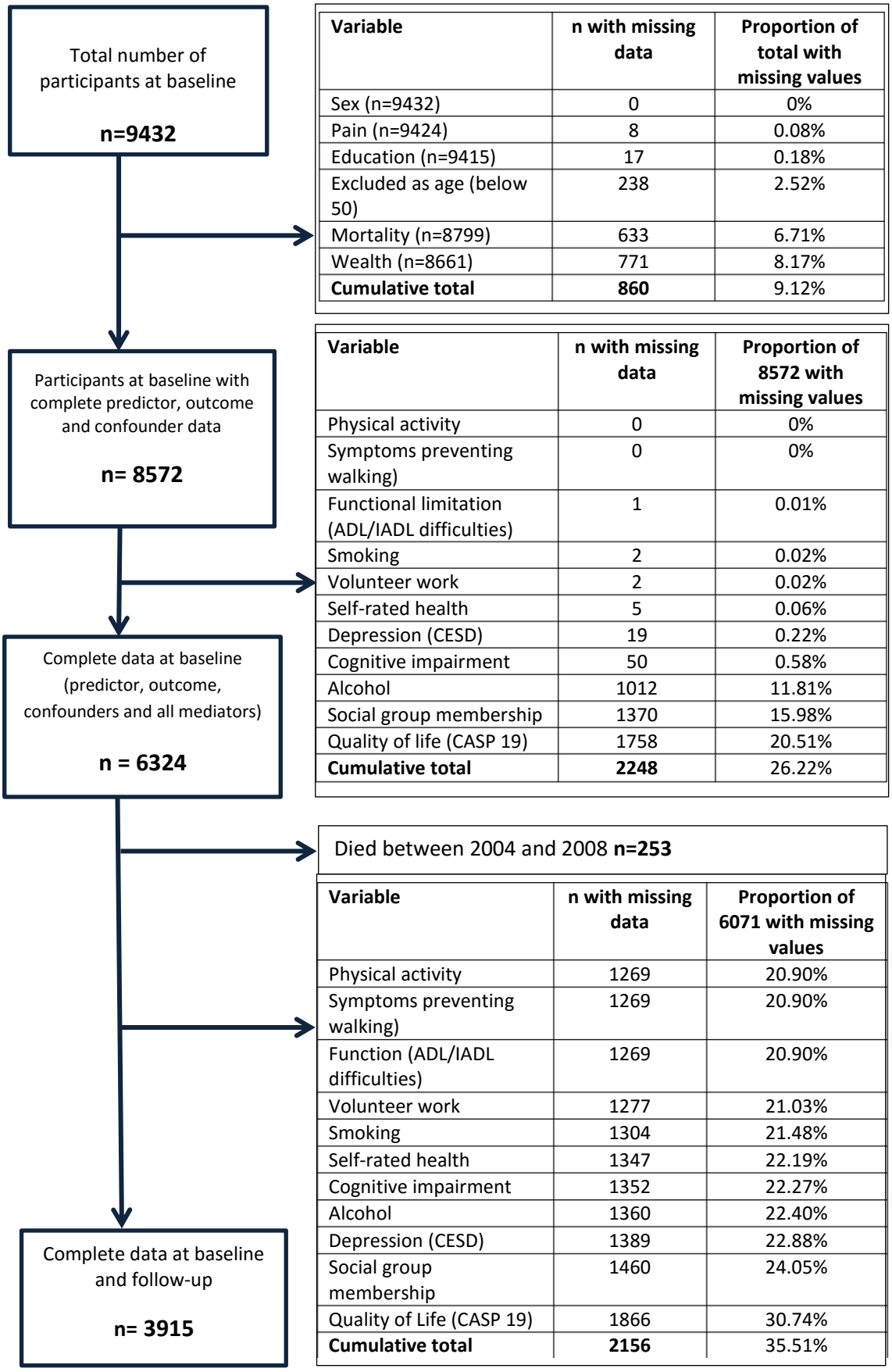


Figure 4.2 Number of participants at each wave of ELSA (Steptoe et al., 2012)

Data collection for Wave 2 took place between June 2004 and July 2005. Participants were included in the analyses if they were age 50 years or over at baseline and had complete data for pain, vital status and proposed mediators, moderators and confounders.

The number of participants for whom information was available at each stage and the proportion of participants with missing data per variable in the ELSA dataset are displayed in Figure 4.3. The variables of allostatic load and frailty are omitted as these factors were treated separately (as described in section 4.6.5). Of the 9432 participants at baseline, 8572 (90.1%) had complete predictor (pain), outcome (vital status) and confounder (age, sex, education and wealth) data and were aged 50 years and over. 238 (2.5%) of the 9432 were aged less than 50 years. Individuals under 50 years were interviewed if they were part of a couple where one member was aged over 50 years. This was to allow the

collection of financial information at benefit unit level where couples keep their finances together. This is considered more useful for considering economic circumstances than using indicators based on the individual (Steptoe et al., 2012). It was also to allow for analyses of intra-couple dynamics regarding health, employment, retirement, and quality of life (Steptoe et al., 2012). This study was not concerned with these issues and was focussed on older adults (50 years and over) so these participants were excluded. Of the 8572 participants with complete predictor, outcome and confounder information, 6324 (67.0% of the total) had complete data for all potential mediators at baseline. At follow up 3915 (41.5%) participants had complete data for all variables (Figure 4.3).



Variable	n with missing data	Proportion of total with missing values
Sex (n=9432)	0	0%
Pain (n=9424)	8	0.08%
Education (n=9415)	17	0.18%
Excluded as age (below 50)	238	2.52%
Mortality (n=8799)	633	6.71%
Wealth (n=8661)	771	8.17%
Cumulative total	**860**	9.12%

Variable	n with missing data	Proportion of 8572 with missing values
Physical activity	0	0%
Symptoms preventing walking)	0	0%
Functional limitation (ADL/IADL difficulties)	1	0.01%
Smoking	2	0.02%
Volunteer work	2	0.02%
Self-rated health	5	0.06%
Depression (CESD)	19	0.22%
Cognitive impairment	50	0.58%
Alcohol	1012	11.81%
Social group membership	1370	15.98%
Quality of life (CASP 19)	1758	20.51%
Cumulative total	**2248**	26.22%

Variable	n with missing data	Proportion of 6071 with missing values
Physical activity	1269	20.90%
Symptoms preventing walking)	1269	20.90%
Function (ADL/IADL difficulties)	1269	20.90%
Volunteer work	1277	21.03%
Smoking	1304	21.48%
Self-rated health	1347	22.19%
Cognitive impairment	1352	22.27%
Alcohol	1360	22.40%
Depression (CESD)	1389	22.88%
Social group membership	1460	24.05%
Quality of Life (CASP 19)	1866	30.74%
Cumulative total	**2156**	35.51%

Figure 4.3 Number and proportion of participants with missing data at each stage of ELSA

4.5.2 NorStOP

At baseline, for the three NorStOP cohorts a total of 26,705 adults aged over 50 years were identified from 8 GP practices in North Staffordshire. 576 (2.2%) were excluded (242 died, 24 were excluded by their GP, 69 withdrew and 241 questionnaires were returned as addressee unknown) either prior to or during the mailing process leaving 26,129 adults eligible for the baseline survey. Of these, 18,497 (70.8%) responded at baseline (Figure 4.4).

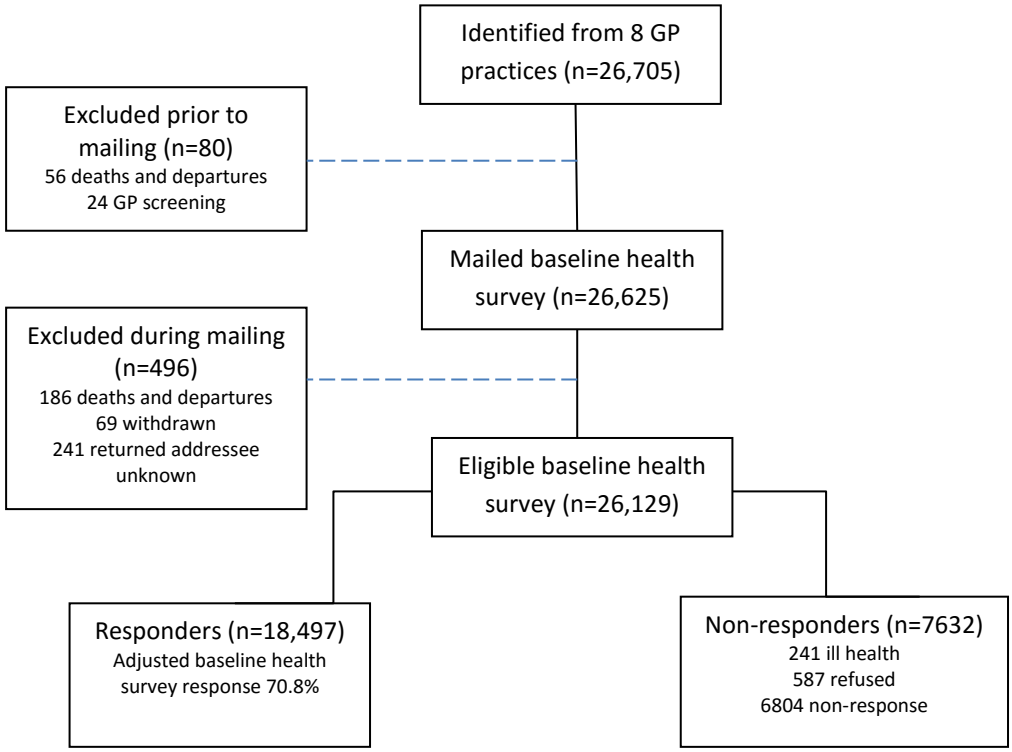
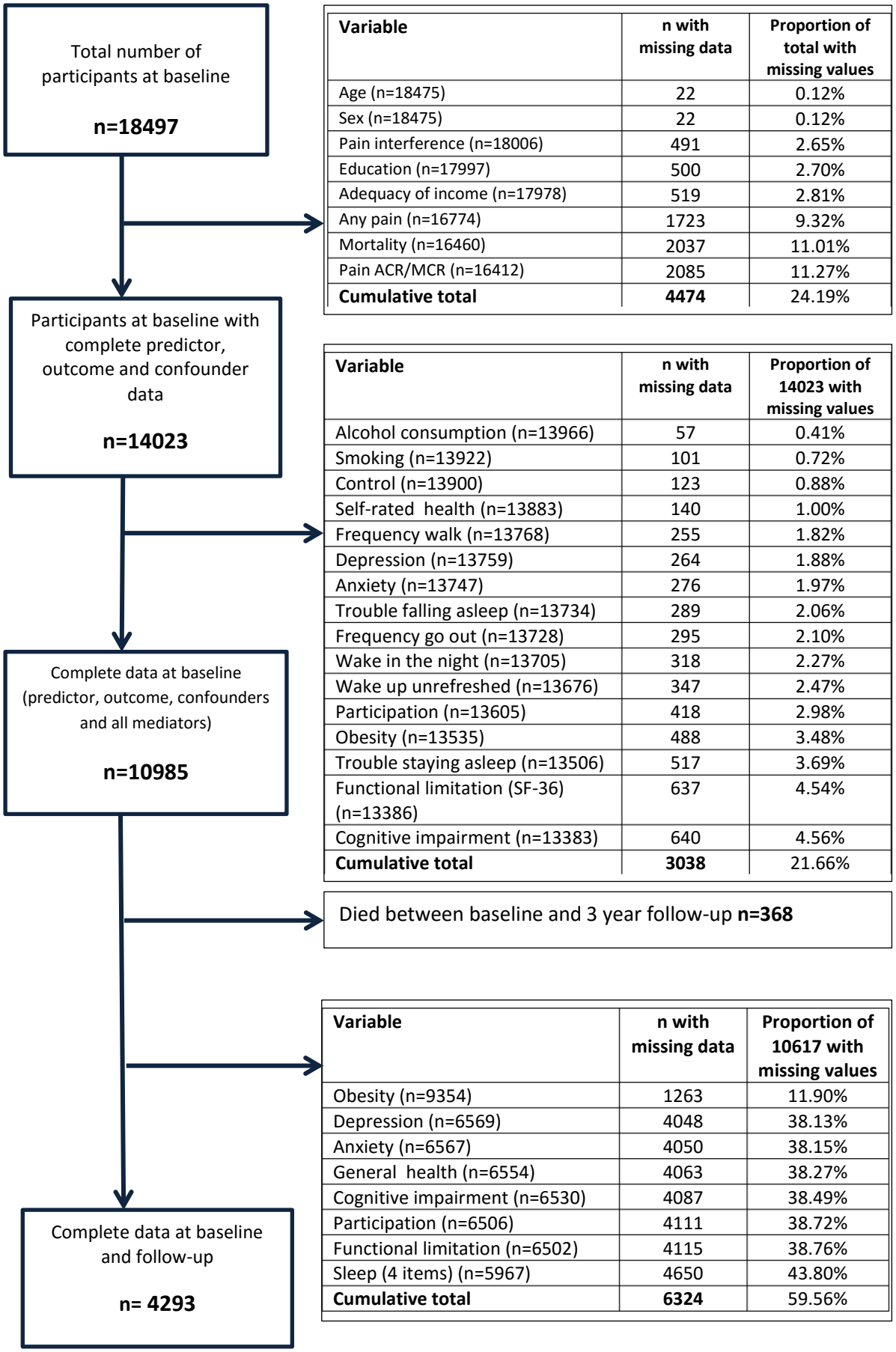


Figure 4.4 Flowchart of baseline response in NorStOP

The number of participants for whom information was available and the proportion of participants remaining at each stage with missing data per variable from the NorStOP dataset are displayed in Figure 4.5. Of the 18,497 participants at baseline 14,023 (75.8%) had complete predictor, outcome and confounder data and 10,985 (59.4%) had



Variable	n with missing data	Proportion of total with missing values
Age (n=18475)	22	0.12%
Sex (n=18475)	22	0.12%
Pain interference (n=18006)	491	2.65%
Education (n=17997)	500	2.70%
Adequacy of income (n=17978)	519	2.81%
Any pain (n=16774)	1723	9.32%
Mortality (n=16460)	2037	11.01%
Pain ACR/MCR (n=16412)	2085	11.27%
Cumulative total	**4474**	24.19%

Variable	n with missing data	Proportion of 14023 with missing values
Alcohol consumption (n=13966)	57	0.41%
Smoking (n=13922)	101	0.72%
Control (n=13900)	123	0.88%
Self-rated health (n=13883)	140	1.00%
Frequency walk (n=13768)	255	1.82%
Depression (n=13759)	264	1.88%
Anxiety (n=13747)	276	1.97%
Trouble falling asleep (n=13734)	289	2.06%
Frequency go out (n=13728)	295	2.10%
Wake in the night (n=13705)	318	2.27%
Wake up unrefreshed (n=13676)	347	2.47%
Participation (n=13605)	418	2.98%
Obesity (n=13535)	488	3.48%
Trouble staying asleep (n=13506)	517	3.69%
Functional limitation (SF-36) (n=13386)	637	4.54%
Cognitive impairment (n=13383)	640	4.56%
Cumulative total	**3038**	21.66%

Variable	n with missing data	Proportion of 10617 with missing values
Obesity (n=9354)	1263	11.90%
Depression (n=6569)	4048	38.13%
Anxiety (n=6567)	4050	38.15%
General health (n=6554)	4063	38.27%
Cognitive impairment (n=6530)	4087	38.49%
Participation (n=6506)	4111	38.72%
Functional limitation (n=6502)	4115	38.76%
Sleep (4 items) (n=5967)	4650	43.80%
Cumulative total	**6324**	59.56%

Figure 4.5 Number and proportion of participants with missing data at each stage of NorStOP

complete data for all proposed mediating factors. At follow up (3 years) only a limited number of the potential mediating factors were measured and only 4293 (23.2%) participants had complete data for all of these mediators at baseline and follow-up (Figure 4.5).

4.6 Missing data

4.6.1 Introduction

The term 'missing data' refers to the absence of information or missing values for a variable of interest (Kang, 2013) and can occur for a number of reasons. Participants may be lost to follow-up over time in a longitudinal study, individuals may not respond to certain questions on a survey as they feel it is not relevant to them, they do not understand the question or they feel it is of a sensitive nature (Goldstein, 2009; Schafer & Graham, 2002). Missing data can be described in terms of unit/whole person non-response where an entire set of data values are missing or as item non-response where individual data values are missing but partial data are available (Schafer & Graham, 2002). Attrition is a term used to describe loss of data from participants over time in a longitudinal study (Goldstein, 2009). Participants may drop out during a study, they may not consent to contact at follow-up time points or they may have moved house or be impossible to contact for another reason (e.g. death, illness).

As described above Figures 4.3 and 4.5 outline the variables for which there were missing data in this study. In ELSA the quality of life measure resulted in the greatest amount of missing data (20.51% at baseline and 30.74% at follow up). This was a composite measure of 22 items; if data for one item was missing a score could not be calculated. Similarly physical function in the NorStOP dataset resulted in a large amount of missing data. This

was measured using the 10 item physical functioning scale of the Short Form (SF)-36 and resulted in 5.54% of missing data at baseline and 38.80% of missing data at follow-up). The greatest amount of missing data at follow up in the NorStOP sample was for the four questions regarding sleep (43.80%). These variables are described in more detail in Section 6 3.3 and Appendix VII.

The implications of missing data are reduced statistical power to detect an existing effect, selection bias in the estimation of parameters (e.g. if data is missing from older participants the resulting estimate will be biased in favour of younger participants as any measure of effect will be calculated from the data of younger participants only which may differ from those of older participants) leading to reduced representativeness of the sample to the target population (the study sample may differ in some way from the target population) and the need for complicated analysis techniques (see below) (Kang, 2013). These factors may threaten the internal and external validity of the study (Kang, 2013).

Missing data can occur by three mechanisms; missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR) (Graham, 2009). Data that is MCAR occurs when the missingness does not depend on the values of observed or missing data (Schafer & Graham, 2002). An example of this would be a blood sample that is accidentally dropped. The reason for missingness is not due to any characteristic of the person from whom the blood was taken nor to any value of any test undertaken on the blood sample. For data that is MAR the missingness depends on values of observed data but not missing data, for example if older people are more likely to have their blood pressure recorded. Data that is MNAR is dependent on values of missing data. An

example of this would be if those with high blood pressure were more likely to have it recorded than those with normal or low blood pressure (Carpenter & Kenward, 2013).

If data is MCAR analysing complete cases will not result in biased parameter estimates but there may not be sufficient power to detect an effect should one exist if there is a large amount of missing data. If data is MAR or MNAR complete case analysis may result in biased estimates (Kang, 2013).

There are a number of techniques available to manage missing data to attempt to reduce potential biases including:

- Listwise deletion which involves discarding any observations with missing values resulting in complete case analysis. This results in a loss of data and can lead to inefficient parameter estimates. It also requires data to be MCAR (Enders & Bandalos, 2001). Listwise deletion has been shown to give unbiased parameter estimates under MCAR but biased estimates under MAR (Kang, 2013).
- Pairwise deletion discards cases on a variable by variable basis and therefore attempts to use all available information. This also requires data to be MCAR (Enders & Bandalos, 2001).
- Weighting is a technique which involves estimation of an effect for a larger sample by weighting the reduced sample according to values of available information in the larger dataset. Each participant is assigned a' sampling weight' which refers to the number of participants in the larger sample that are represented by each participant in the reduced sample (Dunn, Pickles, Tansella, & Vazquez-Barquero, 1999). Weighting can eliminate bias due to differential response on the items used to create the weighting probabilities but cannot correct for biases on items that

are not used or measured (Schafer & Graham, 2002). Further detail regarding this technique is presented in Section 5.5.3.

- Multiple imputation (MI) involves imputing or replacing missing data with a set of plausible values based on the observed data. Several datasets are constructed and analysed separately and their results are combined allowing for the uncertainty introduced as part of the imputation (Clark, Bradburn, Love, & Altman, 2003b). MI assumes missing data is at least MAR (Schafer & Graham, 2002).

Identifying the mechanism of missing data in a study is necessary in order to determine how best to restrict potential biases as a result of that missing data. The procedure undertaken to do this in this study is described below.

4.6.2 Aim

To determine the mechanism of missing data for each sample used in this study from each dataset.

4.6.3 Methods

It is not possible to definitively distinguish between MAR, MCAR and MNAR data (www.missingdata.org.uk) and often in large datasets all three mechanisms of missingness will occur. To examine for the mechanism of missing data logistic regression was used to identify if any of the variables included in the analysis predicted missingness. For each variable with missing data additional binary variables (called indicator variables) were created where values were defined as missing (score of 1) or not missing (score of 0). Correlations between the indicator variables and other variables would indicate the data is MAR (i.e. could be predicted by observed data). If no or low correlations are observed this indicates the data is either MCAR or MNAR (correlation coefficients of less

than 0.35 are generally considered to be low or weak correlations, 0.36 to 0.67 modest or moderate correlations, and 0.68 to 1.0 strong or high correlations (Taylor, 1990)). This whole process was undertaken in Stata 13 using a loop which generated the binary indicator variables and then correlated those variables with all possible variables that may predict the missingness simultaneously, omitting the variable whose indicator is being examined. Details of this method and examples of Stata syntax can be found at "http://www.ats.ucla.edu/stat/stata/seminars/missing_data/mi_in_stata_pt1.htm,". The technique described here helps to provide information about the potential mechanism of missingness which affects the way the data should be treated.

4.6.4 Results

The majority of the coefficients from the correlation analysis to investigate the mechanism of missing data were low (<0.35) for both the ELSA and NorStOP datasets. The complete set of correlations for this analysis can be seen in Appendix III.

4.6.5 Implications

The missingness of variables could not be predicted by the values of observed data which indicated the data were not MAR. Therefore the data were either MCAR or MNAR. It is not possible to determine MNAR as this type of missingness requires information about unobserved values (Schafer & Graham, 2002). As the data in this study were not MAR (required for multiple imputation techniques) and the analysis technique used to perform the mediation analysis (described in Section 6.3.2) would not recognise an imputed dataset, listwise deletion was used to remove those participants with any missing data on

any of the variables to be used in the models. This is a common technique for dealing with missing data which results in complete-case analysis as described above.

In cases where the data can be assumed to be MCAR, complete case analysis produces unbiased estimates and conservative results (Kang, 2013). This technique reduces the size of the sample and subsequently the power to detect an effect where one exists. The amount of missing data at follow up was high in this study (38% missing in the ELSA sample, 61% missing in the NorStOP sample). It was therefore important to calculate the power (to correctly detect an effect where one exists) in the reduced sample sizes.

4.7 Power analysis

4.7.1 Introduction

Larger samples reduce the likelihood of making a type I error (finding an effect where there isn't one) or a type II error (not detecting an effect when one exists) (Jones, Carley, & Harrison, 2003). The probability of a type I error, α, is determined by the researcher and commonly set to 0.05 meaning there is a 5% chance of falsely rejecting a null hypothesis. The power of a test refers to the probability of obtaining a significant result if a real difference exists (denoted by $1-\beta$ where β is the probability of a type II error) (Le, 1997). Generally a power level of 0.8 (80% chance of detecting an existing effect) or above is accepted as sufficient power to detect an existing effect (Jones et al., 2003). Power analysis determines the minimum sample size necessary to detect an effect of a particular size.

4.7.2 Aim

To determine if the following samples had sufficient power to detect the expected effect size for a relationship between pain and mortality:

In ELSA:

i) the baseline sample with complete predictor, outcome and confounder information (n=8572)

ii) the complete case sample at baseline (n=6324)

iii) the complete case sample with complete data at baseline and follow-up (n=3915)

iv) the allostatic load sample at baseline (n=4627) (see section 4.6.5)

v) the allostatic load sample with complete baseline and follow-up data (n=2392) (see section 4.6.5)

vi) the frailty sample at baseline (n=4375) (see section 4.6.5)

vii) the frailty sample with complete baseline and follow-up data (n=2483) (see section 4.6.5)

In NorStOP:

i) the baseline sample with complete predictor, outcome and confounder information (n=14023)

ii) the complete case sample at baseline (n=10985)

iii) the complete case sample with complete data at baseline and follow-up (n=4293)

4.7.3 Methods

In survival analysis, calculations of power are determined by the number of events that take place because censored observations (i.e. those who drop out or who survive until the end of the study period) do not contribute to the power of the test in the proportional hazards model (Hsieh & Lavori, 2000). There are a number of ways to calculate optimum sample sizes in Stata using the stpower command. This command enables the calculation of the number of events and sample size when the power and effect size are known; the calculation of power when the number of events and the effect size are known or the calculation of the effect size when the number of events and power are known. The stpower command is based on the formula by Hseih and Lavori (2000):

$$E = \frac{(z_1 - \alpha/k + z_1 - \beta)^2}{\sigma^2 \beta_1^2 (1 - R^2)}$$

Where E is the total number of events, β_1 is the regression coefficient for the covariate of interest x_1, σ is the standard deviation of x_1, α is the significance level, $\beta$is the probability of a type II error, R^2 is the proportion of variance explained, $z_1 - \alpha/k$ and $z_1 - \beta$ are the (1- α/k)th and the (1-β)th quantiles of the standard normal distribution with k=1 for a one sided test and k=2 for a two sided test (Hseih and Lavori, 2000) (http://www.ats.ucla.edu/stat/stata/seminars/missing_data/mi_in_stata_pt1.htm)).

For all of these tests, the default probability of a type I error (α) was set at 0.05 (Stata Press, 2013). From the literature it was estimated that the approximate mortality rate ratio comparing those with pain to those without pain in English samples would be in the region of 1.3 to 1.4 (Macfarlane et al., 2001; McBeth et al., 2009). As the expected effect size (in this case the mortality rate ratio) and the number of events (observed deaths in each study sample) were known for this study the stpower command was used to calculate the power for each sample listed in the section 4.6.2. Details regarding the methods of collection of mortality data are presented in Section 5.4.

4.7.4 Results from ELSA

Table 4.4 displays the number of deaths in the first three ELSA samples (described in section 4.6.2). For the baseline sample (n=8572) the power to detect a hazard ratio of 1.3 with the probability of a type I error set to 0.05 is 0.998. This means there is a 99.8% chance of detecting an effect of this size should one exist. In this sample it was estimated there was 100% chance of detecting a hazard ratio of 1.4. For the complete case sample (n=6324) there was 95.2% chance of detecting a hazard ratio of 1.3 and 99.6% chance of detecting a hazard ratio of 1.4. However for the complete case sample with follow up data (n=3915) there was only a 44.9% chance of detecting a hazard ratio of 1.3 and 65.2% chance of detecting a hazard ratio of 1.4.

Table 4.4 Power to detect expected hazard ratios per sample size in the achieved samples from the ELSA dataset; α=0.05

Sample	N	Number of events (deaths)	Power	
			Hazard ratio = 1.3	Hazard ratio = 1.4
Baseline (predictor, outcome and confounder information)	8572	1390	0.998	1.000
Complete case	6324	764	0.952	0.996
Complete case plus follow up	3915	195	0.449	0.652

4.7.5 Allostatic load and frailty

The calculation of the indices of allostatic load and frailty required biomarker data collected during the nurse visits (the data used to create these indices along with the method of calculation is described in Chapter 6). This greatly reduced the number of participants for whom data was available and to include these variables in the complete case analysis along with all other variables would have resulted in a drastically reduced

total sample size. The analyses for allostatic load and frailty were therefore presented as separate analyses.

Power calculations were also carried out to determine if there was sufficient power to detect the expected effect size in the allostatic load and frailty samples. In the allostatic load sample (n=4627) there were 567 deaths resulting in an 87.8% chance of detecting a hazard ratio of 1.3 and a 98.0% chance of detecting a hazard ratio of 1.4. In the frailty sample (n=4375) there were 792 deaths resulting in a 95.8% chance of detecting a hazard ratio of 1.3 and a 99.7% chance of detecting a hazard ratio of 1.4 (all α=0.05).

Change over time

Of the participants at baseline with allostatic load data, only 2392 had data at the time of follow up and only 91 participants died. With so few deaths, the power to detect a hazard ratio of 1.3 was only 23.9% and to detect a hazard ratio of 1.4 was only 36.1% (α=0.05).

There were few changes in frailty status between baseline (2004) and follow-up (2008). Including participants who had frailty data at baseline and follow up reduced the sample size to n=2483. Within this group only 169 deaths occurred resulting in 40.0% power to detect a hazard ratio of 1.3 and 59.0% power to detect a hazard ratio of 1.4 (α=0.05).

4.7.6 Results from NorStOP

The results of the power calculations for the NorStOP samples are displayed in table 4.5.

Table 4.5 Power to detect expected hazard ratios per sample size in the achieved samples from the NorStOP dataset; α=0.05

Sample	N	Number of events (deaths)	Power	
			Hazard ratio = 1.3	Hazard ratio = 1.4
Baseline (predictor, outcome and confounder information)	14023	1990	1.000	1.000
Complete case	10985	1484	0.999	1.000
Complete case plus follow up	4293	330	0.664	0.864

It was estimated the baseline sample (n=14023) had 100% chance of detecting a hazard ratio of 1.3 or 1.4. In the complete case sample there was 99.9% chance of detecting a hazard ratio of 1.3 and 100% chance of detecting a hazard ratio of 1.4. In the complete case sample with follow up data there was 66.4% chance of detecting a hazard ratio of 1.3 and 86.4% chance of detecting a hazard ratio of 1.4.

4.7.7 Implications

ELSA

There was insufficient power to identify an association between pain and mortality in the sample with complete data at baseline and follow-up (n=3915) but the sample with all predictor, outcome and confounder information (n=8572) and the complete case sample at baseline (n=6324) were sufficiently powered to detect a hazard ratio of 1.3 or 1.4. The complete case sample (n=6324) was therefore the focus for all subsequent analyses to allow comparison between the survival (described in Chapter Five) and mediation analyses (described in Chapter Six).

The sample size was sufficiently powered to detect a hazard ratio of 1.3 or 1.4 for the allostatic load sample (n=4627) and the frailty sample (n=4375) at baseline. However, as above, there was insufficient power to carry out mediation analysis using change scores between baseline and follow up for those with complete allostatic load data (n=2392) or for those with complete frailty data (n=2483).

NorStOP

For the NorStOP sample the power analysis revealed the sample with all predictor, outcome and confounder information (n=14023) and the sample with all predictor, outcome, confounder and mediator information at baseline (complete case) (n=10985) were sufficiently powered to detect a hazard ratio of 1.3 or 1.4. The complete case (n=10985) was the focus of subsequent NorStOP analyses. There was insufficient power in the sample of participants who had information on mediating factors at both baseline and follow up (n=4293) to detect a hazard ratio of 1.3 but sufficient power to detect a hazard ratio of 1.4.

4.8 Comparisons between samples

4.8.1 Introduction

Although missing data in the current study were assumed to be MCAR (section 4.5) and the complete case samples were therefore considered to be random sub-samples of the larger samples, data that is MCAR is difficult to definitively distinguish. For the current analyses it was possible to investigate the potential for selection bias further by comparing some key characteristics of participants with and without missing mediator data.

4.8.2 Aim

To examine for selection bias by ascertaining if there were statistically significant differences in predictor and confounder information between those with complete data and those with missing mediator data for each sample.

4.8.3 Methods

The participants with complete data at baseline in each dataset (ELSA n=6324, NorStOP n=10985) were compared to the participants with complete predictor and confounder information but missing mediator data (ELSA n=2248, NorStOP n=3038) to determine if there were differences in predictor and confounder information between those with and without missing data. The baseline allostatic load sample (n=4627) and frailty sample (n=4375) from the ELSA dataset were also compared to those with missing allostatic load (n=3945) and frailty (n= 4197) data. Chi-squared tests for binary/categorical variables and the Mann Whitney test for continuous variables (due to non-parametric distribution) were used to test for significant differences between groups (those with and without missing data) in terms of pain phenotype, age, sex, education and wealth (ELSA) or adequacy of income (NorStOP).

4.8.4 Results from ELSA

Table 4.6 displays a comparison between those participants for whom complete baseline data was available (n=6324) and those with missing data (n=2248). Participants with missing data at baseline were significantly more likely to be troubled with pain (43.51% compared to 35.93%, $p<0.001$), have greater severity of pain (moderate pain 22.91%

compared to 18.71%, severe pain 11.61% compared to 6.47%, p<0.001) be older (median age 71 years compared to 63 years, p<0.001), female (58.19% compared to 54.57%, p=0.003), had lower levels of education (5.92% in the highest education category compared to 14.42%, p<0.001) and were financially poorer (11.57% in the highest wealth bracket compared to 23.02%, p<0.001) than those with complete data.

Table 4.6 Comparison of participants with complete data to those with missing mediator data from ELSA

Variable	Complete case at baseline (n=6324)	Participants with missing data (n=2248)	p
Pain			
Not often troubled (reference)	4052 (64.07%)	1270 (56.49%)	
Often troubled	2272 (35.93%)	978 (43.51%)	<0.001[1]
Mild	680 (10.75%)	202 (8.99%	
Moderate	1183 (18.71%)	515 (22.91%)	
Severe	409 (6.47%)	261 (11.61%	<0.001[1]
Age (years)	63 (57-71)*	71 (61-79)*	<0.001[2]
Female	3451 (54.57%)	1308 (58.19%)	0.003[1]
Education			
None	2004 (31.69%)	1314 (58.45%)	
Foreign other	570 (9.01%)	168 (7.47%)	
NVQ1/CSE or equivalent	289 (4.57%	113 (5.03%)	
NVQ2/GCE O level or equivalent	1226 (19.39%)	250 (11.12%)	
NVQ3/GCE A level or equivalent	480 (7.59%)	94 (4.18%)	
Higher education below degree	837 (13.24%)	176 (7.83%)	
NVQ 4/5/Degree or equivalent	918 (14.52%)	133 (5.92%)	<0.001[1]
Wealth (quintiles based on n= 8572 sample)			
Group 1 (lowest)	1011 (15.99%)	703 (31.27%)	
Group 2	1173 (18.55%)	535 (23.80%)	
Group 3	1292 (20.43%)	424 (18.86%)	
Group 4	1392 (22.01%)	326 (14.50%)	
Group 5 (highest)	1456 (23.02%)	260 (11.57%)	<0.001[1]

[1]Chi squared test, [2]Mann Whitney test
Figures refer to n(%), *indicates Median (Inter Quartile Range (IQR))
NVQ = National Vocational Qualification
CSE = Certificate of Secondary Education
GCE= General Certificate of Education

4.8.5 Allostatic load

Table 4.7 displays a comparison between those participants for whom complete allostatic load information was available at baseline (n=4627) compared to those with missing data (n=3945).

Table 4.7 The number and proportion of participants with complete allostatic load data in ELSA at baseline and those with missing data

Variable	Compete allostatic load data at baseline (n=4627)	Participants with missing allostatic load data (n=3945)	p
Pain			
Not often troubled (reference)	2968 (64.15%)	2354 (59.67%)	
Often troubled	1659 (35.85%)	1591 (40.33%)	<0.001[1]
Mild	494 (10.68%)	388 (9.84%)	
Moderate	868 (18.76%)	830 (21.04%)	
Severe	297 (6.42%)	373 (9.46%)	<0.001[1]
Age (years)	65 (58-73)*	65 (57-75)*	0.283[2]
Female	2539 (54.87%)	2220 (56.27%)	0.194[1]
Education			
None	1652 (35.70%)	1666 (42.23%)	
Foreign other	405 (8.75%)	333 (8.44%)	
NVQ1/CSE or equivalent	217 (4.69%)	185 (4.69%)	
NVQ2/GCE O level or equivalent	843 (18.22%)	633 (16.05%)	
NVQ3/GCE A level or equivalent	322 (6.96%)	252 (6.39%)	
Higher education below degree	601 (12.99%)	412 (10.44%)	
NVQ 4/5/Degree or equivalent	587 (12.69%)	464 (11.76%)	<0.001[1]
Wealth (quintiles based on n= 8572 sample)			
Group 1 (lowest)	737 (15.93%)	977 (24.77%)	
Group 2	871 (18.82%)	837 (21.22%)	
Group 3	973 (21.03%)	743 (18.83%)	
Group 4	1038 (22.43%)	680 (17.24%)	
Group 5 (highest)	1008 (21.79%)	708 (17.95%)	<0.001[1]

[1]Chi squared test, [2]Mann Whitney test
Figures refer to n(%), *indicates Median (Inter Quartile Range (IQR))
NVQ = National Vocational Qualification
CSE = Certificate of Secondary Education
GCE= General Certificate of Education

There was a significant difference between those with complete allostatic load data and those who didn't have complete allostatic load data for pain (often troubled and severity), education and wealth (all p<0.001). A lower proportion of participants with complete allostatic load data reported being troubled with pain compared to those with missing data (35.85% compared to 40.33%, p<0.001). They also reported less severe pain (6.42% compared to 9.46%, p<0.001), were more highly educated (12.69% in the highest category compared to 11.76%, p<0.001) and reported greater wealth 21.79% in the highest category compared to 17.95%, p<0.001) than those with missing data. There were no significant differences between the groups for age (p=0.283) or sex (p=0.194).

4.8.6 Frailty

Table 4.8 displays a comparison between those participants for whom frailty information was available at baseline (n=4375) compared to those with missing data for those variables (n=4197) from the original baseline sample (n=8572).

There was a significant difference between those with complete frailty data and those who didn't have complete frailty for pain (often troubled (p=0.003) and severity p<0.001)), age (p<0.001), education (p<0.001) and wealth (p=0.002). A smaller proportion of participants with complete frailty data reported being troubled with pain compared to those with missing data (36.41% compared to 39.48%, p=0.003). They also reported less severe pain (6.42% compared to 9.27%, p<0.001), were less highly educated (10.22% in the highest category compared to 14.39%, p<0.001) and reported greater wealth (20.27% in the highest category compared to 19.75%, p=0.002) than those with missing data. There were no significant differences between the groups according to sex (p=0.209) but those with complete frailty data were significantly older than those with missing frailty

data (median=69 years compared to 58 years, p<0.001). (Note: This was a result of the inclusion of a walking test as part of the frailty index (see section 6.3.3) that was only carried out on participants over 60 years).

Table 4.8 The number and proportion of participants with complete frailty data in ELSA at baseline to those with missing data

Variable	Complete Frailty data at baseline (n=4375)	Participants with missing frailty data (n=4197)	p
Pain			
Not often troubled (reference)	2782 (63.59%)	2540 (60.52%)	
Often troubled	1593 (36.41%)	1657 (39.48%)	0.003[1]
Mild	436 (9.97%)	446 (10.63%)	
Moderate	876 (20.02%)	822 (19.59%)	
Severe	281 (6.42%)	389 (9.27%)	<0.001[1]
Age	69 (64-76)*	58 (55-66)*	<0.001[2]
Female	2400 (54.86%)	359 (56.21%)	0.209[1]
Education			
None	1867 (42.67%)	1451 (34.57%)	
Foreign other	414 (9.46%)	324 (7.72%)	
NVQ1/CSE or equivalent	224 (5.12%)	178 (4.24%)	
NVQ2/GCE O level or equivalent	685 (15.66%)	791 (18.85%)	
NVQ3/GCE A level or equivalent	233 (5.33%)	341 (8.12%)	
Higher education below degree	505 (11.54%)	508 (12.10%)	
NVQ 4/5/Degree or equivalent	447 (10.22%)	604 (14.39%)	<0.001[1]
Wealth (quintiles based on n= 8572 sample)			
Group 1 (lowest)	810 (18.51%)	904 (21.54%)	
Group 2	854 (19.52%)	854 (20.35%)	
Group 3	900 (20.57%)	816 (19.44%)	
Group 4	924 (21.12%)	794 (18.92%)	
Group 5 (highest)	887 (20.27%)	829 (19.75%)	0.002[1]

[1]Chi squared test, [2]Mann Whitney test
Figures refer to n(%), *indicates Median (Inter Quartile Range (IQR))
NVQ = National Vocational Qualification
CSE = Certificate of Secondary Education
GCE= General Certificate of Education

4.8.7 Results from NorStOP

Table 4.9 displays a comparison between those participants for whom baseline mediator information was available (n=10985) compared to those with missing mediator data

(n=3038) according to pain and demographic information. The method of measurement of these variables measured is described in Chapter Five.

Table 4.9 Comparison of participants with complete data to those with missing mediator data in NorStOP

Variable	Complete case at baseline (n=10985)	Participants with missing data (n=3038)	p
Pain			
No (reference)	3166 (28.82%	850 (27.98%)	
Any pain	7819 (71.18%)	2188 (72.02%)	0.363[1]
Pain but not ACR WP	5070 (46.15%)	1413 (46.51%)	
ACR WP	2749 (25.03%)	775 (25.51%)	0.645[1]
Pain but not Manchester WP	6094 (55.48%)	1718 (56.55%)	
Manchester WP	1725 (15.70%)	470 (15.47%)	0.558[1]
Number of pain sites			
0	3197 (29.10%)	865 (28.47%)	
1-3	1953 (17.78%)	609 (20.05%)	
4-6	1942 (17.68%)	517 (17.02%)	
7-11	1833 (16.69%)	497 (16.36%)	
12+	2060 (18.75%)	550 (18.10%)	0.081[1]
Pain interference			
None	3688 (33.57%)	960 (31.60%)	
A little	2899 (26.39%)	723 (23.80%)	
Moderately	1728 (15.73%)	518 (17.05%)	
Quite a bit	2058 (18.73%)	661 (21.76%)	
Extremely	612 (5.57%)	176 (5.79%)	<0.001[1]
Age	63 (56-71)*	66 (58-74)*	<0.001[2]
Female	5967 (54.32%)	1823 (60.01%)	<0.001[1]
Further education	1417 (12.90%)	338 (11.13%)	0.009[1]
Adequacy of income			
Find it a strain	402 (3.66%)	129 (4.25%)	
Have to be careful	4271 (38.88%)	1307 (43.02%)	
Able to manage	4549 (41.41%)	1181 (38.87%)	
Comfortable	1763 (16.05%)	421 (13.86%)	<0.001[1]

[1]Chi squared test, [2]Mann Whitney test
Figures refer to n(%), *indicates Median (Inter Quartile Range (IQR))

Participants with complete data at baseline were significantly more likely to be younger (median 63 years in the complete case sample compared to 66 years in those with missing data, p<0.001), less likely to be female (54.32% in the complete case sample compared to 60.01% in those with missing data, p<0.001), be better educated (12.90% in the highest category compared to 11.13%, p=0.009) and have greater adequacy of

income than those with missing data (16.05% in the 'comfortable' bracket compared to 13.86%, $p<0.001$). They were also significant differences in report of pain interference ($p<0.001$).

4.8.8 Implications

ELSA

Differences between participants with complete data and those with missing data in the ELSA samples reduce the representativeness of the samples to the target population (i.e. the general population of adults aged 50 years and over). Those with missing mediator data were more likely to be troubled with and experience more severe pain. They were more likely to be older, female, less well educated and financially poorer all of which are associated with the report of pain (Breivik et al., 2006; Fillingim et al., 2009; Henschke et al., 2015; Jordan et al., 2008; Macfarlane et al., 2009; Thomas et al., 2007) This underrepresentation of participants who report pain in the complete case sample may mean that if there is a relationship between pain and mortality, the observed relationship in the complete case sample may be an underestimate. For the allostatic load sample there were no differences in age and sex but those with missing data were more likely to be often troubled with pain, experience more severe pain and have lower levels of education and be financially poorer. For the frailty sample participants with missing data were more likely to report troubling pain, be female and financially poorer but were younger and had higher levels of education. The difference in the median age between those with and without missing data is a result of the walking test only being carried out on participants aged over 60 years. This means the risk of mortality in the frailty sample may be higher than would be expected if the sample contained participants aged

between 50 and 60 years. However, it is likely only healthier older adults were able to perform the walking test which would result in an underestimate of the mortality risk. The frailty sample is therefore not a representative sub-sample of the population from which it was derived.

NorStOP

In the NorStOP sample those with missing data were older, more likely to be female, have lower levels of education and be financially poorer, however there were no differences between groups for any of the pain phenotypes with the exception of pain interference. The potential influence of these differences between participants with and without missing mediator data on the observed relationships between pain phenotypes and mortality is unclear but the presence of selection bias indicates the sample may not be representative of the population from which it was derived.

4.9 Comparison of the ELSA and NorStOP baseline complete case samples with national statistics

4.9.1 Introduction

Both the ELSA and NorStOP samples are from the UK population. The ELSA study purports to be representative of the English population and the NorStOP sample representative of North Staffordshire. To ascertain external validity an investigation of whether the derived samples used for this study were representative of the wider national population in terms of age and sex was performed. Comparisons between the complete case samples from each dataset (ELSA n=6324, NorStOP n= 10985) and the population of England and Wales from the 2001 census (Office for National Statistics, 2001) were undertaken.

4.9.2 Aim

To determine if the baseline complete case samples (the main focus for subsequent analyses) were representative of the national (England and Wales) population in terms of age and sex.

4.9.3 Methods

Chi-squared tests were used to test for significant differences in age and sex distribution (overall and according to age band (50-59, 60-69, 70-79 and 80+years)) of participants in the ELSA and NorStOP complete case samples compared to the national population (England and Wales). Looking across age categories allows for a more detailed investigation of the representativeness of the sample as it would highlight potentially important differences in age and sex structure that would be undetectable if considering the sample as a whole. National figures were obtained from the Office of National Statistics 2001 census (Office for National Statistics, 2001).

4.9.4 ELSA

There was a significant difference in the age structure of the ELSA complete case sample and the national population of England and Wales (Chi^2 =278.8; p<0.001) (Table 4.10). The proportion of the ELSA sample aged between 50 and 69 years was lower than in the national population but in total a higher proportion of the ELSA complete case sample were in the two younger age groups compared to the national population (70.3% below age 69 cf 65.6%) and a lower proportion of adults were in the oldest age group (8.2% cf 12.5%).

Table 4.10 Comparison of the ELSA complete case sample (n=6324) with National statistics according to age group			
Age group (years)	**ELSA complete case sample n (%)**	**National statistics (ONS 2001 census) n (Thousands) (%)**	**p**
50-59	2272 (35.9%)	7412.9 (37.7%)	<0.001
60-69	2175 (34.4%)	5488.1 (27.9%)	
70-79	1361 (21.5%)	4310.3 (21.9%)	
80+	516 (8.2%)	2458.6 (12.5%)	
Total	6324 (100.0%)	19669.9 (100.0%)	

Overall, the proportion of men and women in the ELSA complete case sample was similar to the national population (proportion of females: 54.6% cf 54.2%, p=0.304) (Table 4.11). However, within age-strata there were significant differences in the proportion of males and females in the oldest and youngest age groups between the ELSA sample and the national population; there was a greater proportion of females in the youngest age group in the ELSA sample compared to the national population (55.6% cf 50.5%; p<0.001)) and a lower proportion of females in the oldest age group (60.5% cf 67.4%; p=0.002).

Table 4.11 Comparison of the ELSA complete case sample (n=6324) with National statistics according to sex distribution per age group					
Age group (years)	**ELSA complete case sample**		**National statistics (ONS 2001 census) (Thousands)**		**p**
	Male n (%)	**Female n (%)**	**Male n (%)**	**Female n (%)**	
50-59	1010 (44.5%)	1262 (55.5%)	3671.1 (49.5%)	3741.8 (50.5%)	<0.001
60-69	1018 (46.8%)	1157 (53.2%)	2657.4 (48.4%)	2830.7 (51.6%)	0.106
70-79	641 (47.1%)	720 (52.9%)	1881 (43.6%)	2429.3 (56.4%)	0.014
80+	204 (39.5%)	312 (60.5%)	801.8 (32.6%)	1656.8 (67.4%)	0.002
Total	2873 (45.4%)	3451 (54.6%)	9011.3 (45.8%)	10,658.6 (54.2%)	0.304

4.9.5 NorStOP

The age structure of NorStOP complete case was significantly different from the overall the national population (Chi^2=278.8, p<0.001) (Table 4.12). There were higher proportions of participants aged between 50 and 69 years (71.8% cf 65.6%) and a lower

proportion in the 80 years and over group (6.9% cf 12.5%) in the NorStOP sample compared to the national population.

Table 4.12 Comparison of the NorStOP complete case sample (n=10985) with National statistics according to age group			
Age group (years)	**NorStOP complete case sample n (%)**	**National statistics (ONS 2001 census) n (Thousands) (%)**	**p**
50-59	4241 (38.6%)	7412.9 (37.7%)	<0.001
60-69	3648 (33.2%)	5488.1 (27.9%)	
70-79	2336 (21.3%)	4310.3 (21.9%)	
80+	760 (6.9%)	2458.6 (12.5%)	
Total	10985 (100%)	19669.9 (100%)	

Overall the proportion of males and females in the NorStOP sample was similar to the national population (proportion of females: 54.3% cf 54.2%) but there was a significant difference in the proportion of males and females in the youngest age group (proportion of females: 53.2% cf 50.5%; p=0.003) (Table 4.13).

Table 4.13 Comparison of the NorStOP complete case sample (n=10985) with National statistics according to sex distribution per age group					
Age group (years)	**NorStOP complete case sample**		**National statistics (ONS 2001 census) (Thousands)**		**p**
	Male n (%)	**Female n (%)**	**Male n (%)**	**Female n (%)**	
50-59	1985 (46.8%)	2256 (53.2%)	3671.1 (49.5%)	3741.8 (50.5%)	0.003
60-69	1740 (47.7%)	1908 (52.3%)	2657.4 (48.4%)	2830.7 (51.6%)	0.258
70-79	1034 (44.3%)	1302 (55.7%)	1881 (43.6%)	2429.3 (56.4%)	0.322
80+	259 (34.1%)	501 (65.9%)	801.8 (32.6%)	1656.8 (67.4%)	0.240
Total	5018 (45.7%)	5967 (54.3%)	9011.3 (45.8%)	10,658.6 (54.2%)	0.418

4.9.6 Implications

The NorStOP complete case sample was representative of the national population in terms of sex distribution in all age groups apart from in those in the youngest age group. The sex distribution in the youngest and two oldest age groups for the ELSA sample were significantly different from the national population. The higher proportion of females in the younger age group but lower proportion of females in the oldest age groups meant

that overall the sex distribution was not statistically different from the national population, however, the age group structure in both samples was not representative of the national population.

4.10 Discussion

4.10.1 Summary of findings

This chapter introduced the datasets used in this thesis, the response rates to those studies and the samples derived from them for use in this thesis. The mechanisms of missing data were explored and power calculations were undertaken to determine if the samples analysed were of sufficient size to detect the expected size of association between pain and mortality and to ascertain potential sources of bias. The datasets were selected as they provided sufficient information to examine the effect of different phenotypes of pain on the relationship between pain and mortality and the role of potential mediating factors. An examination of the mechanism of missingness for data missing from the complete case samples indicated the complete case sub-samples could be considered as random samples of the larger samples, however a comparison between those with and without mediator data indicated the presence of selection bias. Power analysis confirmed there was sufficient power to detect the expected effect sizes in the complete case samples (ELSA n=6324, allostatic load n=4627, frailty n= 4375, NorStOP n= 10985) but not in follow-up samples for the ELSA complete case analysis (n=3915) or for the allostatic load (n=2392) and frailty samples (n=2483). Only the NorStOP follow-up sample (n=4293) had sufficient power to detect a hazard ratio of 1.4.

Adults over 80 years were underrepresented in both datasets compared to the population of England and Wales, particularly females in the ELSA sample.

4.10.2 Implications

The English Longitudinal Study of Ageing (ELSA) was chosen as it was intended to be a nationally representative dataset and contains data on pain, vital status and a number of potential mediators (of the relationship between pain and mortality) (Steptoe et al., 2012). A criticism of ELSA is that the HSE was used as a sampling frame and this limits participants to those living in private households and excludes those living in residential and nursing homes; which is a common problem with national surveys (Scholes et al., 2008). It is estimated 3.2% of adults in England and Wales aged over 65 years were living in care homes in 2011 (Office for National Statistics, 2014). Care home residents are likely to be older, less healthy and have a higher risk of mortality (Kelfve, Thorslund, & Lennartsson, 2013; Shah, Carey, Harris, Dewilde, & Cook, 2013) therefore any estimate of mortality in community samples is likely to be conservative compared to a population including care home residents.

The North Staffordshire Osteoarthritis project (NorStOP) was chosen as an additional dataset as it included detailed pain data to identify individuals with different pain phenotypes and additional potential mediating factors. Both ELSA and NorStOP are longitudinal studies and are therefore susceptible to attrition. With decreasing sample size at later waves of surveys the precision of the estimates derived from that sample reduce. If non-response is not random the sample may be unrepresentative of the target population, particularly if the reasons for non-response are related to the outcomes of interest (Uhrig, 2008). In the current study the mechanism of missing data and the

potential for selection bias were investigated and reported to ensure this could be considered in the interpretation of the results. Analyses were also only undertaken where it was confirmed there was sufficient power to detect an existing effect reducing the possibility that any findings were a result of chance (Jones et al., 2003).

There were some differences in the age and sex structure of the complete case samples compared to the population of England and Wales but the implications of these differences are difficult to determine. Adjusting for age and sex as potential confounders would minimise the effect of these factors but the presence of other differences between participants with and without missing data may result in the introduction of additional selection bias. It is difficult to definitively determine the effect of missing data on this study as the factors which have missing data are related to both pain and mortality. An advantage of this study is that it investigates the specific role of a number of different factors on the relationship between pain and mortality. Analysis of this kind has not previously been undertaken. The potential mediating factors are assessed individually to determine their effect on the relationship. The use of two different datasets in which some measures are comparable helps to provide a more accurate representation of the influence of those factors.

The sample size was reduced considerably when biomarker information and objective physical characteristics measured at the nurse visit were required to form a composite measure for frailty (n=4375) and allostatic load (n=4637). However, the prevalence of frailty in the ELSA frailty sample (7.54%) was similar to that reported in other studies that have applied the same definition (6.9% (Fried et al., 2001), 6.0% (Gruenewald et al., 2009)). The composite measure of allostatic load is more difficult to compare across

populations as different measures are used to form the index depending on what biomarker information is available and different criteria for scoring the indices are also used. The allostatic load and frailty samples must be considered separately and are not representative of the sample from which they were drawn. The way these composite measures were derived along with a discussion of the strengths and limitations of these measures are presented in Chapter Six.

4.11 Key messages

- This study used two large population based datasets which allowed for the examination of the effect of pain phenotype on the relationship between pain and mortality (Chapter Five) and enabled the investigation of a number of different potentially mediating factors (Chapter Six)
- The mechanism of missing data suggested the complete case samples were random sub-samples of the larger samples but further analysis indicated the presence of selection bias.
- The complete case samples at baseline were of sufficient size to detect the expected effect size in survival analyses.
- The amount of attrition in both the ELSA and NorStOP datasets meant it was not possible to conduct analysis examining the effect of change over time of the mediating factors.

Chapter Five. The influence of pain phenotype on mortality

5.1 Introduction

The relationship between pain and mortality is unclear. One of the key findings of the systematic review described in Chapter Two was that between-study inconsistency in findings may arise from the application of different pain phenotypes across studies. The primary aim of this chapter was to investigate the effect of pain phenotype on the relationship between pain and mortality.

Survival analysis was used to test the relationship between pain phenotype and mortality in the ELSA and NorStOP complete case samples (see Chapter Four for details of these datasets). This chapter presents the definitions of exposures, outcomes and putative confounding variables, the results of the survival analyses, and a critical discussion of the findings.

5.2 Aims

The overall aim of this chapter was to test if the association between pain and mortality was dependent on how pain is defined.

The specific objectives were to test the hypotheses that:

1. Pain is associated with an increased risk of mortality.
2. The relationship would be independent of age, sex and socioeconomic status.
3. The relationship would be dependent on the pain classification used.

5.3 Methods

The main outcome under investigation in this thesis was mortality. Rather than simply assessing whether or not participants died, the time to death can be used to define the mortality risk in terms of the probability of mortality over the period of follow-up. However, not all participants may die in a study, participants may enter the study at different time points and the time to death is unlikely to follow a normal distribution. Survival analysis was developed to deal with these features of data (Clark, Bradburn, Love, & Altman, 2003a) and is described below.

5.3.1 Survival analysis

Survival time and censoring

Survival analysis involves the modelling of survival time, which is the time from a fixed point until a specific event (e.g. death) (Bradburn, Clark, Love, & Altman, 2003; Cox & Oakes, 1984). Participants may enter a study at different times. A participant's survival time is measured from their individual time of entry into the study (as opposed to the date of commencement of the study) until they experience the event in question (Figure 5.1), in this case mortality (Cox & Oakes, 1984).

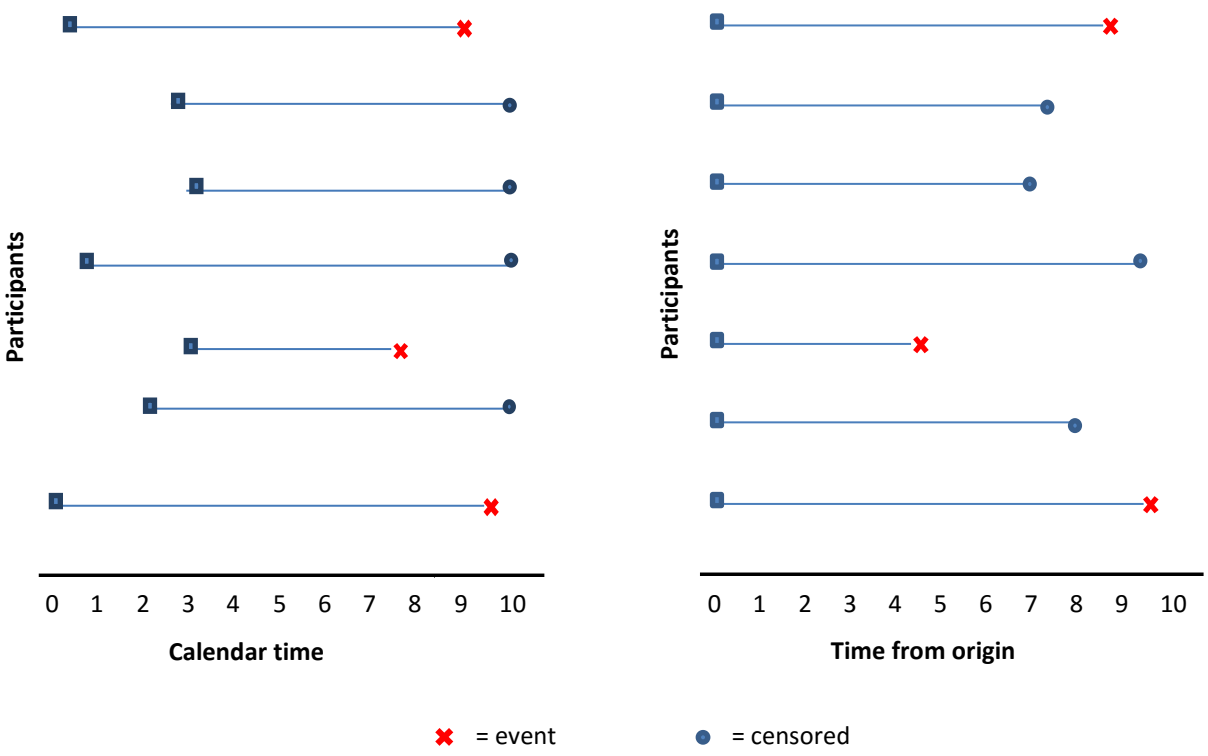


Figure 5.1 Representation of 7 participants with staggered entry and follow up over 10 years in survival analysis (adapted from Cox and Oakes, 1984)

For some participants the survival time is not known; some will survive beyond the end of the follow-up period, some will be lost to follow-up, and for some the experience of a different event makes it impossible for them to be followed-up. This "censoring" of participants should be uninformative, that is those who are censored should have the same survival prospects as those who continue to be followed (Clark et al., 2003a). For example, if those that are censored are unhealthier than those who continue to be observed (i.e. they drop out because they are too sick to continue in the study) the remaining study population would consist of healthier individuals with an increasingly lower risk of mortality and survival would be overestimated (Szklo & Nieto, 2014). The form of censoring where the period of observation ends or the participant 'drops out'

before the event occurs is known as right censoring (Fox, 2002). Other forms of censoring can also occur. Left censoring occurs when the total time at risk is unknown (Fox, 2002); an outcome is observed but it is not possible to determine when it began. One example of left censoring is identifying the reoccurrence of a tumour. If patients have a tumour removed which then regrows soon after but the patient is not examined until three months after the date of removal, the exact time of reoccurrence of the tumour (should it occur within that time period) would be unknown. It would only be possible to say the time to reoccurrence was less than three months (Clark et al., 2003a). Interval censoring occurs when both right and left censoring occur simultaneously, that is, participants come in and out of observation (Fox, 2002). In this study, only participants whose vital status was known by the end of the study time were included so all censored participants were those who survived until the end of the follow-up period.

Analysing differences in survival

Survival data are often described and analysed in terms of survival or hazard probabilities. The survival probability is the probability that an individual survives from the time of origin (i.e.when they enter a study) to a specified future time (e.g the end of the study period) (Clark et al., 2003a). Survival probability can be estimated from the survival times of censored and uncensored participants using the Kaplan Meier (or product limit) method (Kaplan & Meier, 1958). As events (in this case deaths) are assumed to occur independently of each other the probability of surviving from the time of one event to the time of the next event can be multiplied together to give the cumulative survival probability (denoted as S(t)). This can be assessed graphically using a Kaplan Meier curve which shows the survival probability against time (Figure 5.2). The survival curve is drawn

as a step function; that is, the estimated probability changes only at the time of each event and is constant between times of events (Clark et al., 2003a).

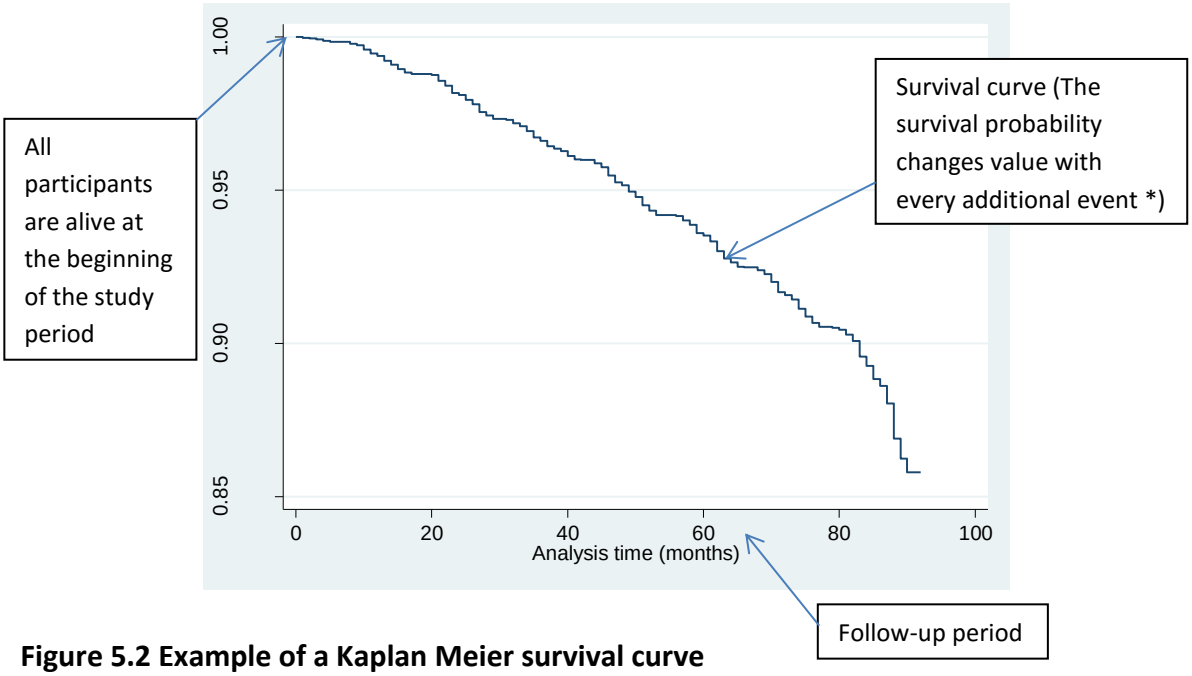


Figure 5.2 Example of a Kaplan Meier survival curve

* Survival probability is calculated for each time point. Censored observations are counted among those who survived until the end of that particular time point but are not included from the number of participants at risk in the next time period.

This method can be used to describe survival according to a factor under investigation and differences in survival curves between groups can be compared using the logrank test. This test compares the number of expected events at each time point in each group if there were no difference between the groups. The total value of expected events is then compared to the number of observed events by calculating a test statistic which is compared to a chi-squared distribution to obtain a p-value to indicate the statistical significance of the difference between survival curves (Clark et al., 2003a). This method does not provide a measure of effect size and does not easily accommodate the impact of other factors such as potential confounders (Bradburn et al., 2003). More complicated multivariate analysis is required to adjust for the impact of other factors (Bradburn et al., 2003; Nieto & Coresh, 1996), the most common of which is the Cox proportional hazard

model (Cox, 1972) which involves use of the hazard function (denoted as h(t)) (Fox, 2002). The hazard function is defined as the instantaneous risk of death (or event in question) at time t, assuming survival to that time (Fox, 2002). There is a clearly defined relationship between the cumulative survival probability (denoted as S(t)) and the hazard function given by the formula:

$$h(t) = -\frac{d}{dt}[\log\ S(t)].$$

Where $h(t)$ = hazard function, $S(t)$ = cumulative survival probability, $\frac{d}{dt}$ =differentiation (change in the slope over time)

The Cox proportional hazard model (Cox, 1972) is a regression model which describes the relationship between an event and a set of covariates expressed by the hazard function (Bradburn et al., 2003). Within the Cox's model, the hazard function is estimated nonparametrically so survival times are not assumed to follow a particular distribution. The formula for the Cox model is:

$$h(t) = h_o(t)\exp\{b_1 x_1 + b_2 x_2 + \cdots + b_p x_p\}$$

Where $h(t)$ = the hazard function, $(x_1, x_2 \ldots x_p)$ = set of covariates $(b_1, b_2, \ldots b_p)$ = size of coefficients $h_o(t)$ = the baseline hazard

The baseline hazard is common to all individuals but is adjusted by the second function; the exponential of the coefficients of the covariates in the model. The hazard function or hazard rate, gives the risk of failure (event) per unit of time (Lee & Wang, 2003) and can be compared across groups of a variable of interest to give a hazard ratio. For example, if comparing group A to group B:

$$\text{Hazard ratio} = \frac{h_A(t)}{h_B(t)}$$

Where $h_A(t)$ = the hazard function in group A and $h_B(t)$ is the hazard function in group B

Where the event in question is mortality, the hazard ratio is referred to as the Mortality Rate Ratio (MRR). A hazard ratio (or MRR) of 1 indicates no difference in the risk of the event in question (or survival) in the comparison group compared to the reference group. Hazard ratios above 1 indicate an increased risk and below 1 indicate a reduced risk at any one point in time (Kay, 2004).

Examining for proportionality

A key assumption of Cox's proportional hazard modelling is that of proportional hazards over time. That is, the hazard in any one group is a constant multiple of the hazard in another so the hazard curves for each group do not cross (Bradburn et al., 2003). If the hazards are not proportional it is inappropriate to use a single hazard ratio to represent the whole follow- up period. It is important to verify this assumption to ensure a proportional hazards model is appropriate. In the analysis used for this study this assumption is tested using the Schoenfeld test which tests for a non-zero slope in a generalised linear regression of scaled Schoenfeld residuals against time (Schoenfeld, 1982). Residuals are the difference between the value predicted by a model and the value observed in the data on which the model is based (Field, 2009). However, the presence of censoring means the usual concept of residuals is not applicable in the proportional hazards model (Lee & Wang, 2003). The Shoenfeld residual is the difference between the observed and expected values conditional on the risk faced by individuals at each time point. Schoenfeld residuals are defined only at uncensored survival times and are set as missing for censored observations (Lee & Wang, 2003). Large residuals indicate the event at time t is unlikely in the model based on the covariates of the individual who died compared to the individuals at risk. Schoenfeld residuals can be plotted against time to test the proportional hazards assumption visually (Schoenfeld, 1982). Deviation from a

straight line indicates a problem with the proportionality assumption as it implies an association between the residuals and time indicating different hazards at different time points (Grambsch & Therneau, 1994). As graphical methods of assessing these assumptions are subjective it is useful to combine them with a statistical test. The null hypothesis for the Schoenfeld test is that that the slope is non-zero, thus rejection of the null hypothesis indicates the proportional hazards assumption does not hold. The test for a non-zero slope implemented in Stata is based on the work of Grambsch and Therneau, (1994) (Grambsch & Therneau, 1994). Tests are performed for each predictor as well as a global test. In a simulation test which examined increasing or decreasing relative hazards, crossing hazards, diverging hazards and non-monotonic hazards, the Schoenfeld test was shown to be one of the most powerful to detect departures from proportionality along with the time dependent covariate test and linear correlation test (compared to score process or omnibus tests) (Ng'andu, 1997). Methods to overcome the problems of non-proportionality include including an interaction term with time or splitting the analysis time into blocks and assessing proportionality within each of those time blocks (BaŞar, 2007).

5.3.2 Applying survival analysis to ELSA and NorStOP data

In analysis of both the ELSA and NorStOP datasets, Cox's proportional hazard modelling was undertaken to assess the risk of death according to pain phenotype (Table 5.1). In order to calculate hazard ratios it was necessary to determine the length of time until the event (in this case death) or censoring takes place. In ELSA, information about vital status was available until the end of February 2012. Only year of death was available for participants in ELSA, therefore the time in the study was calculated in months from the

date of interview until the 31st December in the year the participant was known to have died (or 28th February if they died in 2012). (A request was made to obtain month of death data but this involved an up-front fee of £1000 and permission to use the more detailed mortality data could not be guaranteed so the decision was made to use the available year of death data). The censor date for those who survived was the 28th February 2012. Only participants whose vital status was known were included in the study. In the NorStOP analyses it was possible to calculate the number of days participants remained in the study from the date of questionnaire completion to the date of death or censoring. Information about vital status was available until 1st October 2012. The pain phenotypes investigated are presented in section 5.5.2. The method of data collection for exposures and outcomes is described below.

5.4 Exposures and outcomes

This section describes how information regarding the exposure (pain) and outcome (vital status) were obtained in each dataset. It also describes the data collection methods for the demographic details (age, sex, education and wealth/adequacy of income) which were treated as potential confounders in the survival analysis models.

5.4.1 The English Longitudinal Study of Ageing (ELSA)

Vital status (outcome)

Vital status and cause of death for the ELSA sample was obtained from the Office of National Statistics (ONS). Participants were identified using the National Health Service Central Register (NHSCR), run by the ONS, which keeps track of registrations with general practitioners, with official death registrations and with people who leave the national

health system. The registration of deaths in England and Wales is carried out by the Local Registration Service in partnership with the General Register Office (GRO). Information is usually supplied by an informant, who is often a close relative, and cause of death is obtained from the Medical Certificate of Cause of Death (MCCD) which is completed by a medical practitioner when the death is certified. The ONS record the underlying cause of death identified by a four digit code from the Tenth Revision of the International Classification of Diseases and Related health problems (ICD-10). Automatic validation checks on variables such as date of death, sex, year of birth and marital status which highlight inconsistencies are undertaken once the deaths are recorded in the ONS database. The underlying cause of death is coded automatically for the majority of deaths (approximately 80%) with the remainder being coded manually by experienced coders (Mortality Statistics in England and Wales, 2013). 95% of participants gave consent for their records to be accessed so most of the deaths recorded in ELSA were confirmed by the NHSCR. For the remaining participants deaths were reported by relatives of the deceased or by interviewers who learned of deaths when trying to make contact with the household (Banks, Breeze, Lessof, & Nazroo, 2006). In ELSA cause of death was grouped according to 1) the three most common causes of death: cancer, cardiovascular diseases, respiratory diseases, 2) known causes other than the most common ("other") or 3) unknown cause of death ("unknown").

Pain (predictor)

Participants were asked whether they were often troubled with pain and responded "yes" or "no". Those who responded "yes" were then asked how bad their pain was most of the time with the response options of 'mild', 'moderate' or 'severe'. Previous studies have recorded the presence and location of pain (Andersson, 2009; Macfarlane et al., 2007;

Macfarlane et al., 2001; McBeth et al., 2009) and some have also included a measure of chronicity (Sjøgren & Grønbæk, 2010; Smith et al., 2003; Torrance et al., 2010). It was not possible to determine the extent or duration of pain in this dataset.

Confounders

Demographic variables were included in the current analysis as confounders. They were age, sex and socio-economic status indicated by educational attainment and current wealth. These are all factors which are associated with both pain and mortality (described in Section 1.5).

Age and sex

For age and sex, participants were asked to confirm their sex and date of birth. If they did not know their date of birth they were asked what their age was on their last birthday. Age was categorised into year bands 50-59, 60-69, 70-79 and 80+; a standard method of categorising age that has been used in other studies (Dreyer et al., 2010; Kamiya, Whelan, Timonen, & Kenny, 2010; Thomas et al., 2007).

Education and wealth

Socioeconomic position is a complex construct (Galobardes et al., 2006). Education is often used as a measure of socioeconomic status as it can help determine a person's occupation and income in adulthood. It reflects access to and performance in school/college/university in childhood and young adulthood hence it captures early life circumstances and the influence of adult resources (Galobardes et al., 2006). A measure of education can also reflect a number of non-socioeconomic factors pertinent to health research such as health-related knowledge and health literacy (Braveman et al., 2005). However, education should not be used as a sole measure of socioeconomic position as

income levels can vary greatly at similar educational levels especially across different social groups (e.g. sex, age, ethnic) reflecting different levels of access to material resources (Braveman et al., 2005). In older adults, wealth is considered to be a good indicator of socioeconomic status. It reflects an accumulation of economic resources and an ability to withstand periods of low income which may result from unemployment or illness (Braveman et al., 2005). In the current analysis, measures of education and wealth were both included as measures of socioeconomic status.

For educational attainment in ELSA, participants were asked to look at a card listing educational qualifications and indicate which, if any, they held. The highest educational level attained was categorised according to the following categories; National Vocational Qualification (NVQ)4/5 or degree or equivalent, higher education below degree, NVQ3/A level equivalent, NVQ2/O level equivalent, NVQ1/Certificate of Secondary education (CSE) or equivalent or foreign/other or no qualification. For wealth, net total non-pension wealth, was categorised by using quintiles to provide five groups labelled from low to high. Five categories were considered adequate to capture information contained in a continuous variable and minimise bias due to a loss of information that may arise due to the sub-categorisation (Cochran, 1968). The quintiles were empirically defined based on the distribution. The wealth variable was measured at business unit level which represents an individual or couple along with any dependent children (as opposed to individual wealth alone). It is calculated from answers to questions regarding house or property wealth, businesses and any form of savings or investment minus any debt (Steptoe et al., 2012). This measure of wealth has been found to be the strongest

socioeconomic predictor of health in the ELSA sample (Demakakos, Nazroo, Breeze, & Marmot, 2008).

5.4.2 The North Staffordshire Osteoarthritis Project (NorStOP)

Vital status (outcome)

Information regarding participants' vital status was collated from two sources. Firstly, data was obtained from the Exeter patient registration system held at the local Primary Care Trust in October 2012. The Exeter system is a database of all patients registered with a GP in England and Wales. It is used to trace people as they move and register with a new GP and to calculate payments to GP practices. Patients are removed from the register if they emigrate or die. In recording deaths, the date of death is the only information required (http://staffs-sbs.nhs.uk/registration/faqs/#faq58). Secondly, these dates were supplemented with the dates of death notified to the NorStOP project team during the six year follow up period. Manual tracing of the NHS Summary Care Record Demographic system was used to confirm the dates notified to the project team. Participants whose vital status could not be confirmed in 2012 were excluded from the dataset ensuring that the vital status of all participants was known. Days in the study were calculated from the date of response to the questionnaire until the date of death or until census date (1st October 2012).

Pain (predictor)

A filter question was used which asked participants "In the past 4 weeks have you had pain that has lasted for one day or longer in any part of your body (not including pain from illnesses such as flu)?" Response options were "yes/no". Responders were categorised into those with bodily pain and those without. Responders who indicated

that they had body pain were asked to shade their painful areas on a full body manikin (front and back views) (see Figure 5.3).

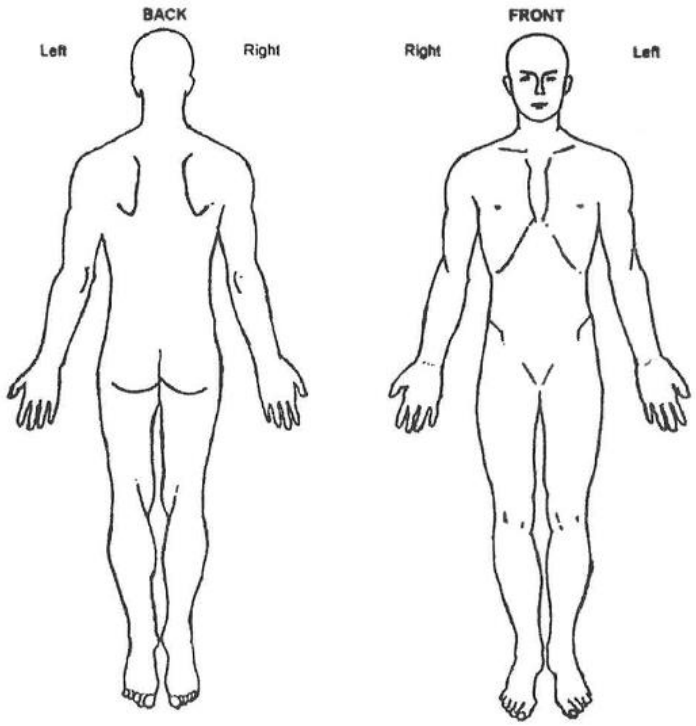


Figure 5.3 NorStOP Manikin

Five phenotypes of pain were derived from the NorStOP dataset:

Any pain

Based on the filter question participants who responded “yes” were categorised as having “any pain”. This question was used to determine the presence of pain, irrespective of whether participants had indicated the site of their pain on the blank body manikin. Those participants who indicated ‘yes’ to the filter question but indicated no sites on the manikin were classified as having pain. If participants indicated ‘no’ to the filter question but did shade parts of the manikin they were classified as having no pain.

Widespread pain

1. American College of Rheumatology (ACR) criteria

The location of pain indicated on the manikin was used to classify whether or not participants met the ACR criteria (pain in the axial skeleton, on the right and left sides of the body and above and below the waist) for widespread pain (Wolfe et al., 1990). The ACR criteria are a widely used method of capturing widespread pain and have been used in other studies investigating pain and mortality (Macfarlane et al., 2001; McBeth et al., 2009).

2. Manchester criteria

Manikin data was also used to determine if participants met the Manchester criteria for widespread pain (pain in both the axial skeleton and at least two sections of two contralateral limbs) (described in Section 1.4) (Hunt et al., 1999).

Number of pain sites

A template dividing the body into 44 sites (Figure 5.4) was used to provide a count of the number of shaded areas on the body manikin from which a number of pain sites variable was constructed. This was divided into five categories; no sites of pain, 1-3 sites, 4-6 sites, 7-11 sites and 12+ sites of pain. These categories have been used previously in NorStOP as they contained approximately equal numbers of people in each category (Thomas, Peat, et al., 2004). (Detail regarding single and multi-site pain is presented in Section 1.4.2).

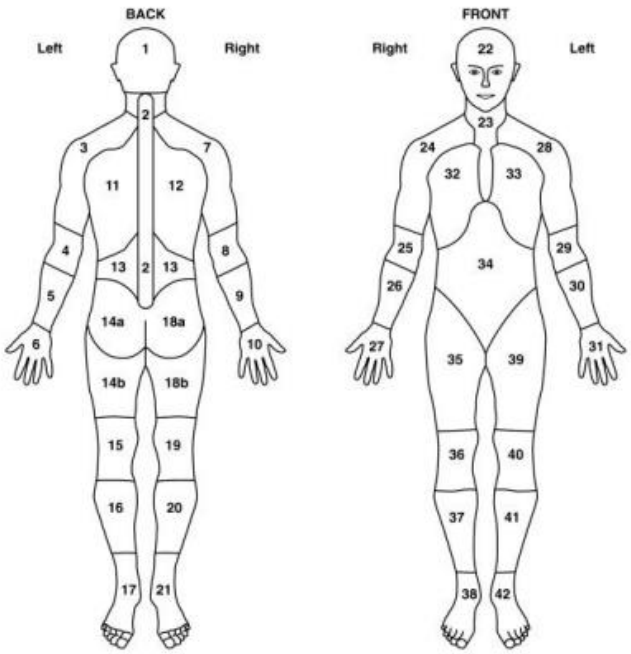


Figure 5.4 NorStOP template for calculating pain sites/widespread pain

Pain interference

A single item from the Medical Outcomes Study (MOS) Short Form (SF)-12 (Ware, Kosinski, & Bayliss, 1995) was used as a measure of current interference of pain in everyday life. All participants were asked: "During the past 4 weeks how much did pain interfere with your normal work (including both work outside the home and housework)?" There were 5 available responses to the question: 'Extremely', 'Quite a bit', 'Moderately', 'A little bit' or 'Not at all'. This single item has been used in previous population studies as a measure of pain interference (Blyth et al., 2001; Teh et al., 2009) and is associated with increasing age (Thomas et al., 2007; Thomas, Peat, et al., 2004) and a reduction in social networks (Peat et al., 2004) in the NorStOP dataset. The reference group for this item in the survival analysis was 'no pain interference' which included participants who indicated they had pain but this did not interfere with their life.

Demographic details

Information about age, sex, education and adequacy of income were collected and used as potential confounders. Education and adequacy of income were included as a measure of socioeconomic status.

Age and sex

Participants were asked to confirm their sex and date of birth to enable the calculation of their current age. Age was categorised into to the year bands 50-59, 60-69, 70-79 and 80+ in line with the approach applied to the ELSA data.

Education and adequacy of income

Measures of education and financial resources were again used to capture the multidimensional nature of socioeconomic position. To assess educational attainment participants were asked to indicate whether they had continued full-time education beyond school (response options 'yes/no') which formed a dichotomous variable indicating school education/further education. Although this item lacks detail regarding specific qualifications it provides information regarding different levels of educational attainment (high (further education) or low (school education only)) for comparison and is comparable to the measure used in ELSA which included school level and further education qualifications. Perceived adequacy of income was measured with a single item. Participants were asked to think about the cost of living as it affected them and describe their situation using one of the following responses:

1) Find it a strain to get by from week to week
2) Have to be careful with money
3) Able to manage without much difficulty
4) Quite comfortably off

It measures a range of financial circumstances (from affluence to poverty) without eliciting details of responders' income. This item was developed by Thomas (1999) and provides an account of whether the responder feels that they are under financial strain (Thomas, 1999). Perceived adequacy of income has been demonstrated to be a robust indicator of financial capacity in older adults (Litwin & Sapir, 2009).

5.5 Statistical analysis

5.5.1 Sample characteristics

The ELSA sample consisted of those participants who had complete data for the predictor (pain), outcome (vital status), confounder (age, sex, education and wealth) and for all proposed mediators (apart from allostatic load and frailty) (see Table 4.1). This was referred to as the ELSA complete case sample (n=6324). The NorStOP sample included participants with complete predictor (pain), outcome (vital status), confounder (age, sex, education and adequacy of income) and mediator information (see table 4.2) (n=10985) and is referred to as the NorStOP complete case sample.

First of all, the complete case samples from ELSA and NorStOP were described according to demographic, socioeconomic, lifestyle, health, social and psychological factors (the method of data collection for the included lifestyle, health, social and psychological factors is described in Section 6.3.3). The samples were then stratified according to vital status. Chi-squared or Mann Whitney tests (for non-parametric distributions) were undertaken where appropriate to determine differences between those participants who died and those who remained alive at the end of the study period.

5.5.2 Survival analysis

Cox's proportional hazard modelling (see section 5.3.1) was used to test the risk of all-cause mortality and cause-specific mortality (ELSA only) according to pain phenotype. The phenotypes examined are displayed in Table 5.1.

Table 5.1 Pain phenotypes tested for their relationship with mortality

Dataset	Pain phenotype	Reference group	Categories
ELSA	**"Often troubled"**	Not often troubled with pain	1) often troubled
ELSA	**Severity**	Not often troubled with pain	1) Mild 2) Moderate 3) Severe
NorStOP	**"Any pain"**	No pain	1) "any pain"
NorStOP	**ACR criteria**	No pain	1) Pain not meeting ACR WP 2) ACR WP
NorStOP	**Manchester criteria**	No pain	1) Pain not meeting Manchester WP 2) Manchester WP
NorStOP	**Number of pain sites**	No pain sites (equivalent to 'no pain')	1) 1-3 sites 2) 4-6 sites 3) 7-11 sites 4) 12+ sites
NorStOP	**Pain interference**	No pain interference	1) 'a little' 2) 'moderately' 3) 'quite a bit' 4) 'extremely'

NorStOP = North Staffordshire Osteoarthritis Project
ELSA = English Longitudinal Study of Ageing
ACR = American College of Rheumatology
WP = Widespread Pain

In ELSA it was also possible to examine the effect of pain phenotype (often troubled and severity) on cause-specific mortality. Analyses were undertaken to assess the risk of mortality from cancer, cardiovascular disease and respiratory disease, other causes of death and unknown causes of death.

All analyses are presented as unadjusted “crude” analyses (Model 1) and then cumulatively adjusted for age and sex (Model 2) and education and wealth (ELSA)/adequacy of income (NorStOP) (Model 3). The results of the Cox’s proportional hazard models are presented as Mortality Rate Ratios (MRRs) with 95% confidence intervals (CI).

5.5.3 Weighting

There are a number of practical disadvantages when using longitudinal surveys, in particular non-response and attrition at subsequent waves resulting in a reduced sample size. Mechanisms of missing data (e.g. missing at random) and some ways of dealing with it (e.g. imputation) are described in Section 4.5.1. One way to examine the sensitivity of the relationship of interest (in this case the association between pain and mortality) to participant attrition and missing data is to complete a probability weighted analysis. The analysis in Chapter Four indicated there were differences between those with complete data and those with missing data. An investigation of whether weighted analysis could be used in order to represent those with missing data (that could also be used in the mediation analysis) was undertaken.

Weighting involves the removal of participants with incomplete data from the dataset and the subsequent weighting of the remaining complete cases so that the distribution of the reduced sample resembles the full sample with respect to specified variables (Schafer & Graham, 2002). Each participant in the complete case sample is assigned a number representing a ’sampling weight’. This refers to the number of participants in the original (full) sample who were eligible to provide a response that are represented by each individual participant in the reduced (complete case) sample who did provide a response

(Dunn et al., 1999). These weights represent the probability of response and are determined from the full sample using logistic regression. It is possible to weight responses using information from the complete case sample in a similar way to using data from the second phase of a two phase survey by deeming all participants who responded (complete data) as representative of all participants who were eligible to respond. For example if 60 out of a possible 100 participants have complete data, a sampling weight can be assigned to those 60 to additionally represent the 40 who did not complete the data. In this case, the sampling weight would be the inverse of the sampling fraction (i.e.100/60= 1.67) (Dunn et al., 1999).

In the ELSA sample weights were calculated from the age, sex, education and wealth variables. These variables were used to calculate the weights as they were potential confounders in the analysis and were used to determine differences between the complete case samples and those with missing mediator data. Binary variables for age (above and below the median), wealth (above and below the median) and education (further education or not) were created. For the NorStOP sample the variables were dichotomised in the same way but perceived adequacy of income replaced wealth and was dichotomised as “find it a strain/have to be careful with money versus little difficulty/comfortable”. Participants scored 1 if they were female, in the oldest age category and highest wealth/income and education categories. Altogether sixteen combinations of these categories were possible. The number of participants in each of these categories was counted in each of the samples. Weights for each of the sixteen categories were calculated by dividing the number in the smaller (complete case) sample by the number in the larger sample (including those with missing mediator data) and

adding one. These figures were then used to form a weighting variable to weight the complete case sample to the baseline sample with predictor, outcome and confounder information only. That is, each participant in the complete case sample was allocated one of the 16 weight values to indicate how many baseline sample participants were represented by each participant based on the combination of those variables.

The survival analyses to examine the risk of mortality according to pain phenotype were undertaken in the weighted samples by including the weighting variable in the survival models as an additional covariate. The weighted results were then compared to the results of the complete case samples. There were no differences between the MRRs in the weighted analyses and the complete case samples for either the ELSA or the NorStOP datasets (Appendix IV). The focus of all subsequent analyses was therefore the unweighted complete case samples for each dataset. The results of the survival analyses for the baseline samples with predictor, outcome and confounder information only and the weighted analyses can be seen in Appendix IV.

5.5.4 Assumption testing

The assumption of proportionality for the Cox's models was tested using Schoenfeld tests for the crude (Model 1) and fully adjusted models (Model 3) and plots of Schoenfeld residuals (see section 5.3.1). Results of these are presented in Appendix V. Survival probability for each pain phenotype was also presented graphically using Kaplan Meier plots.

5.6 Results of the descriptive analysis

5.6.1 The ELSA complete case sample

Sample characteristics

Table 5.2 presents descriptive characteristics of the complete case sample for the ELSA dataset and a comparison between those participants who died and those who did not before the end of the study. Participants who died during 8 years of follow-up (n=764) compared to those who remained alive (n=5560) were older, more likely to be male and of lower socioeconomic status (i.e. lower education and wealth). Participants who died were also more likely to be often troubled with pain, report greater severity of pain, lower physical activity levels, poorer self-rated health and quality of life, more likely to smoke, drink less alcohol, report functional limitation and symptoms preventing walking. Participants who died also had more depressive symptoms and greater cognitive impairment, were less likely to undertake volunteer work and were members of fewer social groups, were more likely to report the presence of any comorbidity and each of the four categories of comorbidities (p<0.001 for all comparisons) (Table 5.2).

Table 5.2 Characteristics of the ELSA complete case sample overall and stratified by vital status

Variable	Total (n=6324)	Alive (n=5560)	Dead (n=764)	p
PAIN				
Often troubled with pain				
No (reference)	4052 (64.07%)	3624 (65.18%)	428 (56.02%)	
Yes	2272 (35.93%)	1936 (34.82%)	336 (43.98%)	<0.001[1]
Severity				
Mild	680 (10.75%)	620 (11.15%)	60 (7.85%)	
Moderate	1183 (18.71%)	982 (17.66%)	201 (26.31%)	
Severe	409 (6.47%)	334 (6.01%)	75 (9.82%)	<0.001[1]
DEMOGRAPHICS				
Age (years)				
50-59	2272 (35.93%)	2204 (39.64%)	68 (8.90%)	
60-69	2175 (34.39%)	2019 (36.31%)	156 (20.42%)	
70-79	1361 (21.52%)	1081 (19.44%)	280 (36.65%)	
80+	516 (8.16%)	256 (4.60%)	260 (34.03%)	<0.001[1]

Sex				
Female	3451 (54.57%)	3105 (55.85%)	346 (45.29%)	<0.001[1]
Education				
None	2004 (31.69%)	1658 (29.82%)	346 (45.29%)	
Foreign/other	570 (9.01%)	478 (8.60%)	92 (12.04%)	
NVQ1/CSE or equivalent	289 (4.57%)	243 (4.37%)	46 (6.02%)	
NVQ2/GCE O level or equivalent	1226 (19.39%)	1140 (20.50%)	86 (11.26%)	
NVQ3/GCE A level or equivalent	480 (7.59%)	434 (7.81%)	46 (6.02%)	
Higher education below degree	837 (13.24%)	771 (13.87%)	66 (8.64%)	
NVQ 4/5/Degree or equivalent	918 (14.52%)	836 (15.04%)	82 (10.73%)	<0.001[1]
Wealth (quintiles based on n = 8572 sample)				
Group 1 (lowest)	1011 (15.99%)	796 (14.32%)	215 (28.14%)	
Group 2	1173 (18.55%)	1011 (18.18%)	162 (21.20%)	
Group 3	1292 (20.43%)	1160 (20.86%)	132 (17.28%)	
Group 4	1392 (22.01%)	1252 (22.52%)	140 (18.33%)	
Group 5 (highest)	1456 (23.02%)	1341 (24.12%)	115 (15.05%)	<0.001[1]
LIFESTYLE FACTORS				
Physical activity at least once a week				
None	377 (5.96%)	248 (4.46%)	129 (16.89%)	
Mild	859 (13.58%)	678 (12.19%)	181 (23.69%)	
Moderate	3125 (49.42%)	2787 (49.24%)	338 (44.24%)	
Vigorous	1963 (31.04%)	1847 (33.22%)	116 (15.18%)	<0.001[1]
Smoking				
Never	2361 (37.33%)	2159 (38.83%)	202 (26.44%)	
Ex-smoker	3053 (48.28%)	2633 (47.36%)	420 (54.97%)	
Current smoker	910 (14.39%)	768 (12.14%)	142 (18.59%)	<0.001[1]
Alcohol in the last 12 months				
Less than weekly	2313 (36.58%)	1970 (35.43%)	343 (44.90%)	
Weekly or more	4011 (63.43%)	3590 (64.57%)	421 (55.11%)	<0.001[1]
HEALTH FACTORS				
Self-reported health				
Excellent	886 (14.01%)	844 (15.18%)	42 (5.50%)	
Very good	1927 (30.47%)	1793 (32.25%)	134 (17.54%)	
Good	2031 (32.12%)	1779 (32.00%)	252 (32.98%)	
Fair	1098 (17.36%)	879 (15.81%)	219 (28.67%)	
Poor	382 (6.04%)	265 (4.77%)	117 (15.31%)	<0.001[1]
Functional limitation				
Difficulties with activities of daily living (0-13)	0 (0-0)*	0 (0-0)*	0 (0-2)*	<0.001[2]
>1 indicated difficulty	1554 (24.57%)	1188 (21.37%)	366 (47.91%)	<0.001[1]
Symptoms preventing walking (0-13)	0 (0-0)*	0 (0-0)*	1 (0-2)*	<0.001[2]
>1 symptom	1483 (23.45%)	1077 (19.37%)	406 (53.14%)	<0.001[1]

Comorbidity				
Cancer	182 (2.88%)	118 (2.12%)	64 (8.38%)	<0.001[1]
Cardiovascular disease	2307 (36.48%)	1971 (35.45%)	336 (43.98%)	<0.001[1]
Respiratory disease	685 (10.83%)	570 (10.25%)	115 (15.05%)	<0.001[1]
Other	2011 (31.80%)	1698 (30.54%)	313 (40.97%)	<0.001[1]
No comorbidity	2585 (40.88%)	2365 (42.54%)	220 (28.80%)	
Any comorbidity	3739 (59.12%)	3195 (57.46%)	544 (71.20%)	<0.001[1]
SOCIAL FACTORS				
Volunteer work				
No	4363 (68.99%)	3757 (67.57%)	606 (79.32%)	
Yes	1961 (31.01%)	1803 (32.43%)	158 (20.68%)	<0.001[1]
Social group membership (0-8)	1 (1-2)*	1 (1-2)*	1 (0-2)*	<0.001[2]
PSYCHOLOGICAL FACTORS				
Quality of Life (CASP-19)				
Control (0-12)	9 (7-10)*	9 (7-11)*	7 (5-9)*	<0.001[2]
Autonomy (0-15)	11 (9-13)*	11 (9-13)*	10 (8-12)*	<0.001[2]
Pleasure (0-15)	14 (13-15)*	14 (13-15)*	14 (12-15)*	<0.001[2]
Self-realisation (0-15)	11 (8-13)*	11 (9-13)*	9 (6-11)*	<0.001[2]
Total (0-57)	44 (38-50)*	45 (39-50)*	40 (33-46)*	<0.001[2]
Depression (CESD) (0-8)	3 (2-4)*	3 (2-4)*	3(2-4)*	<0.001[2]
Depression (binary)				
<4 depressive symptoms	4619 (73.04%)	4161 (74.84%)	458 (59.95%)	
=>4 depressive symptoms	1705 (26.96%)	1399 (25.16%)	306 (40.05%)	<0.001[1]
Cognitive impairment				
Number of words recalled (0-20)	11 (8-13)*	11 (9-13)*	9 (6-11)*	<0.001[2]

CASP= Control, Autonomy, Self-realisation and Pleasure scale
CESD=Centre for Epidemiologic Studies Depression scale
NVQ = National Vocational Qualification
CSE = Certificate of Secondary Education
GCE= General Certificate of Education

[1] Chi squared test, [2] Mann Whitney test
Figures refer to n(%), * indicates Median (Inter Quartile Range (IQR))

5.6.2 The NorStOP complete case sample

Sample characteristics

Participants who died in the NorStOP complete case sample were more likely to be older, male, of lower socioeconomic status (measured according to education and income ($p<0.001$ for all comparisons)), more likely to report pain interference ($p<0.001$), sleep

problems (trouble falling asleep p=0.005, wake in the night p<0.001, trouble staying asleep p=0.031, wake up unrefreshed p=0.014), participation restriction (p<0.001) and be obese (p<0.001). Participants who died were also less likely to go out (p<0.001) or walk for 10 minutes (p<0.001), have lower self-rated health (p<0.001), greater functional limitation (p<0.001), higher depressive symptoms (p<0.001), greater cognitive impairment (p<0.001) and reported less control over their health (p=0.001). However, participants who died were less likely to be current smokers (p<0.001) and drank alcohol less frequently (p<0.001) than those who remained alive. There were no statistically significant differences in the report of any pain (p=0.333), ACR WP (p=0.155), Manchester WP (p=0.627), number of pain sites (p=0.201) or anxiety (p=0.247) between those who died and those who remained alive (Table 5.3).

Table 5.3 Descriptive characteristics of the total NorStOP complete case sample and stratified according to mortality status

Variable	Total (n=10985)	Alive (n=9501)	Dead (n=1484)	p
PAIN				
No (reference)	3166 (28.82%)	2754 (28.99%)	412 (27.76%)	
Any pain	7819 (71.18%)	6747 (71.01%)	1072 (72.24%)	0.333[1]
Pain but not ACR WP	5038 (45.86%)	4324 (45.51%)	714 (48.11%)	
ACR WP	2749 (25.03%)	2397 (25.23%)	352 (23.72%)	0.155[1]
Missing[+]	32 (0.29%)	26 (0.27%)	6 (0.40%)	
Pain but not Manchester WP	6062 (55.18%)	5235 (55.10%)	827 (55.73%)	
Manchester WP	1725 (15.70%)	1486 (15.64%)	239 (16.11%)	0.627[1]
Missing[+]	32 (0.29%)	26 (0.27%)	6 (0.40%)	
Number of pain sites				
0	3166 (28.82%)	2754 (28.99%)	412 (27.76%)	
1-3	1952 (17.77%)	1707 (17.97%)	245 (16.51%)	
4-6	1942 (17.68%)	1666 (17.53%)	276 (18.60%)	
7-11	1833 (16.69%)	1592 (16.76%)	241 (16.24%)	
12+	2060 (18.75%)	1756 (18.48%)	304 (20.49%)	0.201[1]
Missing	32 (0.29%)	26 (0.27%)	6 (0.40%)	
Pain interference				
None	4501 (40.97%)	4002 (42.12%)	499 (33.63%)	
A little	2316 (21.08%)	2089 (21.99%)	227 (15.30%)	
Moderately	1562 (14.22%)	1328 (13.98%)	234 (15.77%)	
Quite a bit	2004 (18.24%)	1634 (17.20%)	370 (24.93%)	

Extremely	602 (5.48%)	448 (4.72%)	154 (10.38%)	<0.001[1]
DEMOGRAPHICS				
Age (years)				
50-59	4241 (38.61%)	4086 (43.01%)	155 (10.44%)	
60-69	3648 (33.21%)	3300 (34.73%)	348 (23.45%)	
70-79	2336 (21.27%)	1766 (18.59%)	570 (38.41%)	
80+	760 (6.92%)	349 (3.67%)	411 (27.70%)	<0.001[1]
Sex				
Female	5967 (54.32%)	5275 (55.52%)	692 (46.63%)	<0.001[1]
Further Education				
Yes	1417 (12.90%)	1298 (13.66%)	119 (8.02%)	<0.001[1]
Adequacy of income				
Find it a strain	402 (3.66%)	360 (3.79%)	42 (2.83%)	
Have to be careful	4271 (38.88%)	3638 (38.29%)	633 (42.65%)	
Able to manage	4549 (41.41%)	3924 (41.30%)	625 (42.12%)	
Comfortable	1763 (16.05%)	1579 (16.62%)	184 (12.40%)	<0.001[1]
LIFESTYLE FACTORS				
Smoking				
Never/Previous	7099 (64.62%)	6049 (63.67%)	1050 (70.75%)	
Current	3886 (35.38%)	3452 (36.33%)	434 (29.25%)	<0.001[1]
Alcohol				
Monthly or less	4660 (42.42%)	3939 (41.465)	721 (48.58%)	
Weekly	6325 (57.58%)	5562 (58.54%)	763 (51.42%)	<0.001[1]
Obesity				
Yes	2093 (19.05%)	1863 (19.61%)	230 (15.50%)	<0.001[1]
Frequency go out				
All days	3557 (32.38%)	3325 (35.00%)	232 (15.63%)	
Most days	3486 (31.73%)	3096 (32.59%)	390 (26.28%)	
Some days	2468 (22.47%)	2056 (21.64%)	412 (27.76%)	
Few days	1236 (11.25%)	904 (9.51%)	332 (22.37%)	
No days	238 (2.17%)	120 (1.26%)	118 (7.95%)	<0.001[1]
Frequency walk for 10 minutes				
Every day	1599 (14.56%)	1462 (15.39%)	137 (9.23%)	
Every other day	2146 (19.54%)	1936 (20.38%)	210 (14.15%)	
Twice a week	2452 (22.32%)	2220 (23.37%)	232 (15.63%)	
Less than weekly	2285 (20.80%)	1987 (20.91%)	298 (20.08%)	
Never	2503 (22.79%)	1896 (19.96%)	607 (40.90%)	<0.001[1]
Sleep				
Trouble falling asleep				
Some/none	9563 (87.06%)	8305 (87.41%)	1258 (84.77%)	
Most nights	1422 (12.94%)	1196 (12.59%)	226 (15.23%)	0.005[1]
Wake in the night				
Some/none	8454 (76.96%)	7423 (78.13%)	1031 (69.47%)	
Most nights	2531 (23.04%)	2078 (21.87%)	453 (30.53%)	<0.001[1]
Trouble staying asleep				
Some/none	8871 (80.76%)	7703 (81.08%)	1168 (78.71%)	
Most nights	2114 (19.24%)	1798 (18.92%)	316 (21.29%)	0.031[1]
Wake up unrefreshed				
Some/none	9204 (83.79%)	7993 (84.13%)	1211 (81.60%)	
Most nights	1781 (16.21%)	1508 (15.87%)	273 (18.40%)	0.014[1]

HEALTH FACTORS				
Self-rated health				
Excellent	436 (3.97%)	413 (4.35%)	23 (1.55%)	
Very good	2653 (24.15%)	2468 (25.98%)	185 (12.47%)	
Good	4490 (40.87%)	3998 (42.08%)	492 (33.15%)	
Fair	2750 (25.03%)	2180 (22.94%)	570 (38.41%)	
Poor	656 (5.97%)	442 (4.65%)	214 (14.42%)	<0.001[1]
SOCIAL FACTORS				
Social participation restriction (KAP)				
None	5879 (53.52%)	5337 (56.17%)	542 (36.52%)	
Any	5106 (46.48%)	4164 (43.83%)	942 (63.48%)	<0.001[1]
Functional limitation (SF36)	75 (45- 90)*	80 (50-95)*	45 (15-80)*	<0.001[2]
PSYCHOLOGICAL FACTORS				
Anxiety (HADS)				
No	6914 (62.94%)	6000 (63.15%)	914 (61.59%)	
Possible/probable	4071 (37.06%)	3501 (36.85%)	570 (38.41%)	0.247[1]
Depression (HADS)				
No	8918 (81.18%)	7874 (82.88%)	1044 (70.35%)	
Possible/probable	2067 (18.82%)	1627 (17.12%)	440 (29.65%)	<0.001[1]
Cognitive impairment				
No	6330 (57.62%)	5656 (59.53%)	674 (45.42%)	
Yes	4655 (42.38%)	3845 (40.47%)	810 (54.52%)	<0.001[1]
Control (from IPQ-R)				
Disagree	7916 (72.06%)	6792 (71.49%)	1124 (75.74%)	
Agree	3069 (27.94%)	2709 (28.51%)	360 (24.26%)	0.001[1]

IQR = Inter Quartile Range
ACR = American College of Rheumatology
WP = Widespread Pain
KAP = Keele Assessment of Participation
SF 36 = Short Form 36
HADS = Hospital Anxiety and Depression Scale
IPQ-R = Illness Perception Questionnaire (Revised)

[1] Chi squared test, [2] Mann Whitney test
Figures refer to n(%), * indicates Median (Inter Quartile Range (IQR))
[+] the complete case samples were based on those responding to the filter question regarding 'any pain'

5.7 Results of the survival analysis

5.7.1 Often troubled with pain (ELSA) and mortality

Tests of proportionality

For the ELSA complete case sample (n=6324) the length of time in the study for those who died (n=764) ranged from 0 months to 90 months from the date of interview with a mean survival time of 54.1 months (SD 24.7). 5.2% (n = 40) of deaths occurred within 12 months from the date of interview. For "often troubled" with pain the result of the Schoenfeld tests were not statistically significant in the crude model (Model 1) (often troubled with pain compared to not often troubled (Chi^2=2.48 p=0.11)) or in the fully adjusted model (Model 3). The global test was also not statistically significant for Model 3 indicating the association between "often troubled" with pain and mortality was constant across the 8 years of follow up. The assumption of proportionality was therefore considered to be valid. Results of the Schoenfeld tests for Model 3 and the plots of the Schoenfeld residuals can be seen in Appendix V.

Survival probability over time

The rate of mortality was higher in those often troubled with pain when compared to those not often troubled with pain (Figure 5.5).

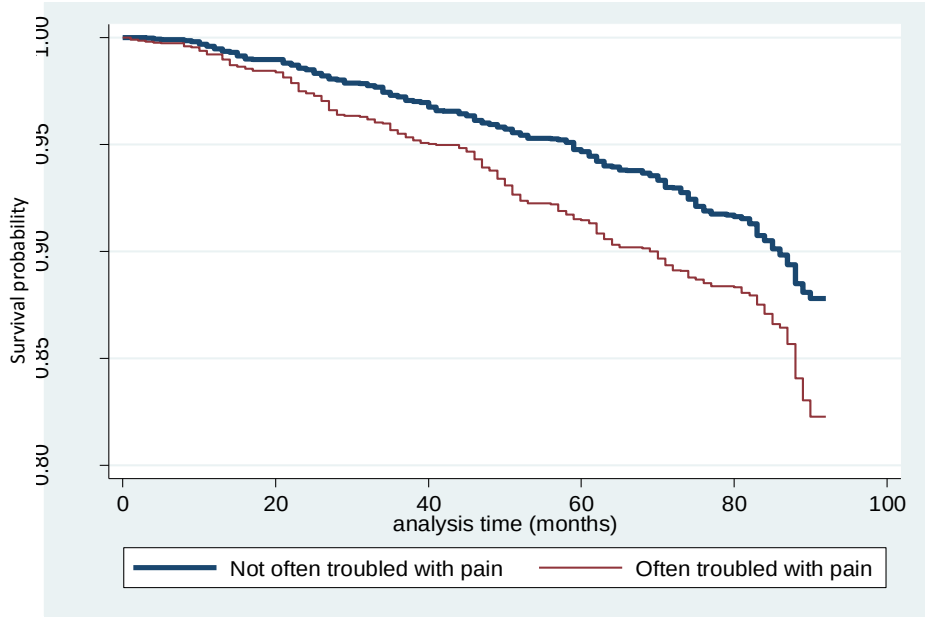


Figure 5.5 Survival probability over 92 months for often troubled with pain and those not often troubled by pain; Kaplan Meier plots in the ELSA complete case sample (n=6324)

Mortality risk

Those "often troubled" with pain had a 43% increased risk of mortality when compared to those not "often troubled" with pain (Model 1: MRR 1.43; 95%CI 1.24, 1.65) and this remained significant when adjusted for age and sex (Model 2: MRR1.36; 95%CI 1.18, 1.58) and for age, sex, education and wealth (Model 3: MRR 1.29; 95%CI 1.12, 1.49) (Table 5.4).

5.7.2 Severity of pain (ELSA)

Tests of proportionality

For severity of pain the Schoenfeld tests for the crude (Model 1) and fully adjusted (Model 3) models were not statistically significant indicating the assumption of proportionality was valid (Appendix V).

Survival probability over time

When the relationship between pain severity and mortality was examined, it was clear that the rate of mortality was highest in those with moderate and severe pain (Figure 5.6).

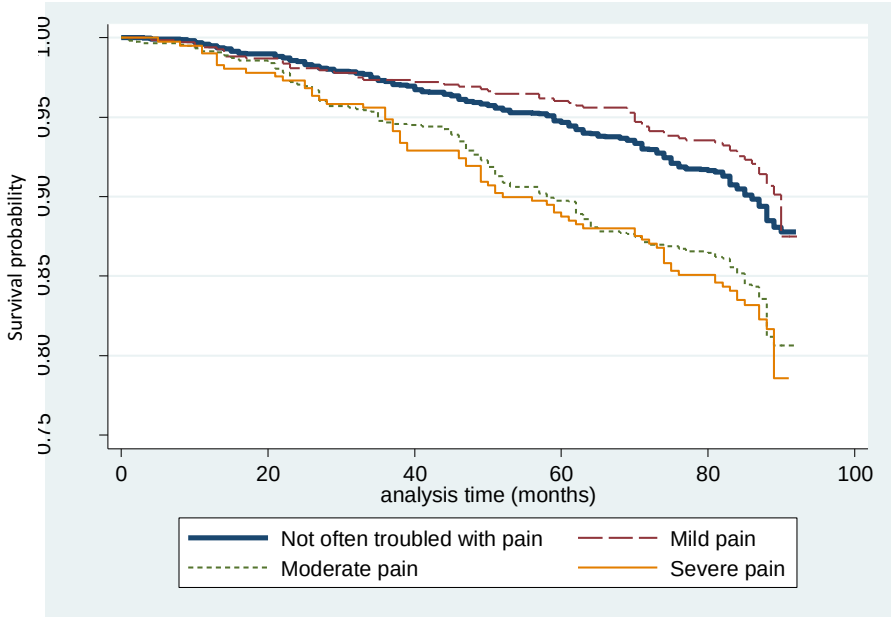


Figure 5.6 Survival probability over 92 months for levels of pain severity; Kaplan Meier estimates in the ELSA complete case sample (n=6324)

Mortality risk

When compared to those reporting they were not "often troubled" with pain, participants who reported mild pain were not more likely to die over the follow up period (MRR 0.83; 95%CI 0.63, 1.09). However participants reporting moderate (MRR 1.65; 95%CI 1.40, 1.95) or severe (MRR 1.81; 95%CI 1.41, 2.31) pain had a 70% and 80% increased risk of death. The association between moderate and severe pain and a higher risk of mortality attenuated slightly when adjusted for age and sex (Model 2: moderate pain: MRR 1.52; 95%CI 1.28, 1.80, severe pain: MRR 1.42; 95%CI 1.20, 1.68) and when adjusted for age, sex, education and wealth (Model 3: moderate pain: MRR 1.42; 95%CI

1.20, 1.68, severe pain: MRR 1.54; 95%CI 1.20, 1.97) although the elevated risk persisted and remained significant (Table 5.4).

5.7.3 Any pain (NorStOP)

Tests of proportionality

In the NorStOP analysis (n=10985), the length of time in the study for participants who died (n=1484) ranged from 7 days to 3823 days from the date of response with a mean survival time of 2036 days (SD 1052). 6.54% (n=97) of deaths occurred within 12 months from the date of response.

The results of the Schoenfeld test for the crude model (Model 1) for "any pain" (Chi^2=2.74, p=0.098) and the fully adjusted model (Model 3) (Chi^2=9.63, p=0.086) were not statistically significant indicating the assumption of proportionality was valid (Appendix V).

Survival probability over time

Survival probability over time was lower across the study period for those with "any pain" compared to those with no pain (Figure 5.7).

Table 5.4 Risk of all-cause mortality in the ELSA complete case sample according to pain phenotype (n=6324)							
Pain phenotype	**N**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
Not often troubled	4052	28048	428	15.26	Reference	Reference	Reference
Often troubled	2272	15414	336	21.80	**1.43 (1.24, 1.65)**	**1.36 (1.18, 1.58)**	**1.29 (1.12, 1.49)**
Not often troubled	4052	28048	428	15.26	Reference	Reference	Reference
Mild	680	4737	60	12.67	0.83 (0.63, 1.09)	0.87 (0.66, 1.14)	0.89 (0.68, 1.16)
Moderate	1183	7943	201	25.31	**1.65 (1.40, 1.95)**	**1.52 (1.28, 1.80)**	**1.42 (1.20, 1.68)**
Severe	409	2734	75	27.43	**1.81 (1.41, 2.31)**	**1.70 (1.33, 2.18)**	**1.54 (1.20, 1.97)**

MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education and wealth
***per 1000 person-years**
MRRs in bold indicate significant associations

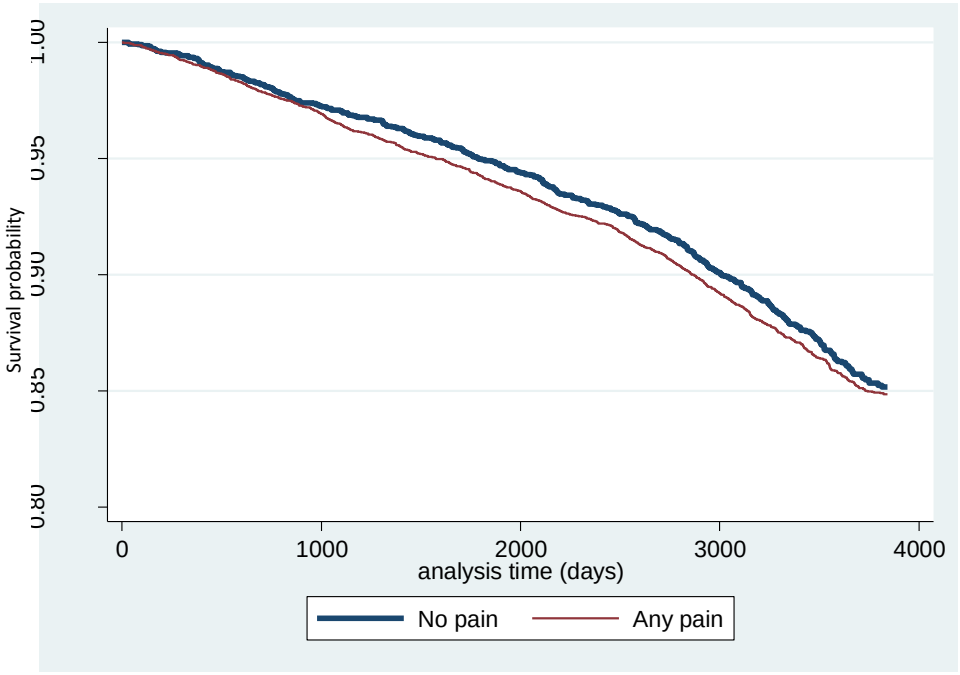


Figure 5.7 Survival probability over 10 years for any pain and those with no pain; Kaplan Meier plots in the NorStOP complete case sample (n=10985)

Mortality risk

There was no statistically significant increased risk of mortality for participants with "any pain" (Model 1: MRR 1.05; 95%CI 0.94, 1.18) which demonstrated minimal change after adjustment for potential confounders (Model 2: MRR 1.08; 95%CI 0.96, 1.21, Model 3: MRR 1.06; 95%CI 0.95, 1.19) (Table 5.5).

5.7.4 ACR WP (NorStOP)

Tests of proportionality

For ACR WP criteria the Schoenfeld test for Model 1 (Chi^2=2.84, p=0.241) and Model 3 (Chi^2=9.64, p=0.141) were not statistically significant indicating the assumption of proportionality was reasonable (Appendix V).

Survival probability over time

Survival probability for those with ACR WP was similar to that for those with no pain; survival probability for those with pain that did not meet the ACR criteria was lower than for those with widespread pain (Figure 5.8).

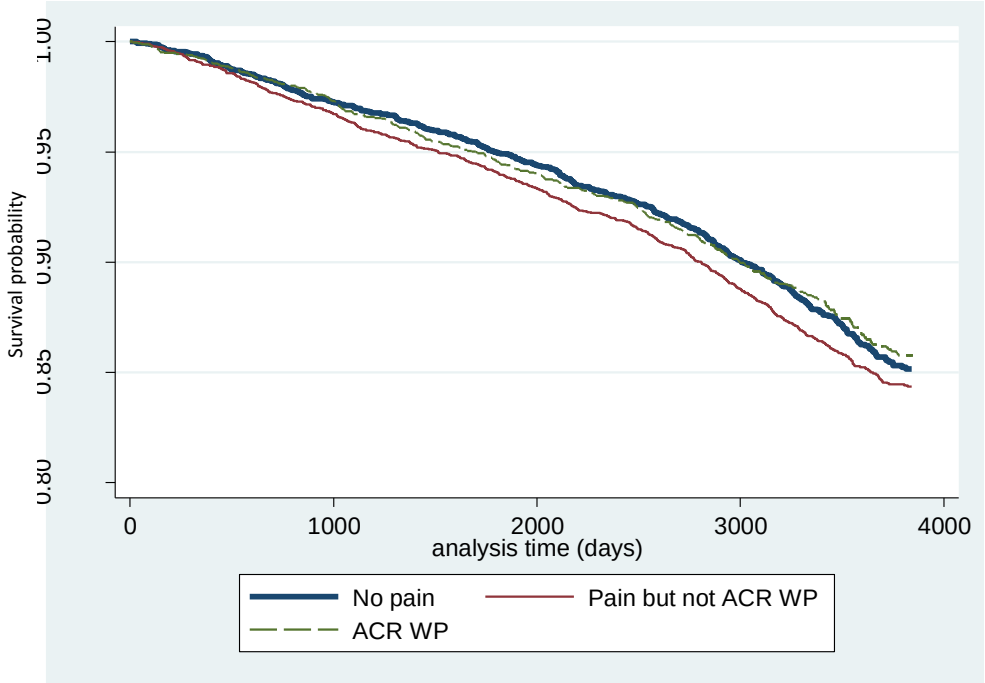


Figure 5.8 Survival probability over 10 years for American College of Rheumatology Widespread Pain (ACR WP) criteria; Kaplan Meier estimates in the NorStOP complete case sample (n=10953)

Mortality risk

There was no statistically significant increased risk of mortality for participants with pain that was not ACR WP (Model 1: MRR 1.09; 95%CI 0.97, 1.23, Model 2: MRR 1.06; 95%CI 0.94, 1.20, Model 3: MRR 1.05; 95%CI 0.93, 1.19) or for participants with ACR WP (Model 1: MRR 0.97; 95%CI 0.85, 1.12, Model 2: MRR 1.10; 95%CI 0.95, 1.26, Model 3: MRR 1.07; 95%CI 0.92, 1.23) (Table 5.5).

5.7.5 Manchester WP (NorStOP)

For Manchester WP criteria the Schoenfeld tests for Model 1 (Chi^2=4.50, p=0.105) and Model 3 (Chi^2=12.45, p=0.053) were not statistically significant indicating the risk of mortality was proportional over time.

Survival probability over time

The survival probability for those with Manchester WP was lower than for those with no pain or pain that did not meet the Manchester criteria for widespread pain (Figure 5.9).

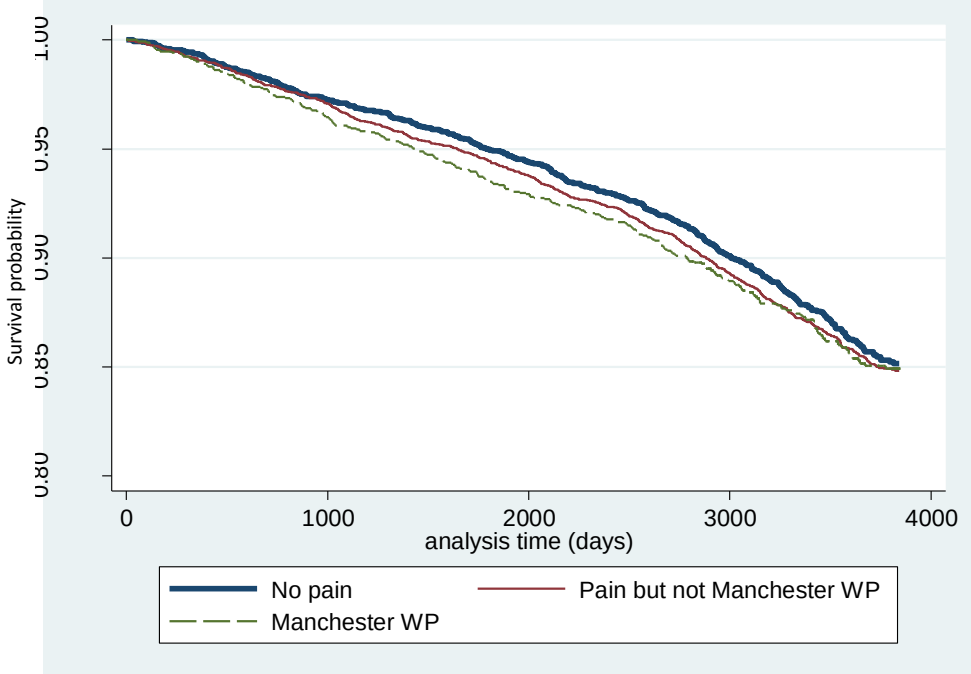


Figure 5.9 Survival probability over 10 years for Manchester Widespread Pain criteria (Manchester WP); Kaplan Meier estimates in the NorStOP complete case sample (n=10953)

Mortality risk

For participants with Manchester WP there was an increased risk of mortality in the analyses adjusted for age and sex only (Model 2: MRR 1.19; 95%CI 1.02, 1.40). There was

no statistically significant increased risk of mortality for pain that was not Manchester WP (Table 5.5).

5.7.6 Number of pain sites (NorStOP)

Tests of proportionality

For the number of pain sites the Schoenfeld test for Model 1 (Chi^2=6.36, p=0.174) and Model 3 (Chi^2=13.24, p=0.104) indicated the proportionality assumption was valid.

Survival probability over time

There was no trend between increasing number of pain sites and survival probability. Survival probability was lowest in those with 12+ sites but those with 7-11 sites of pain had a similar survival probability over time to those reporting no pain (Figure 5.10).

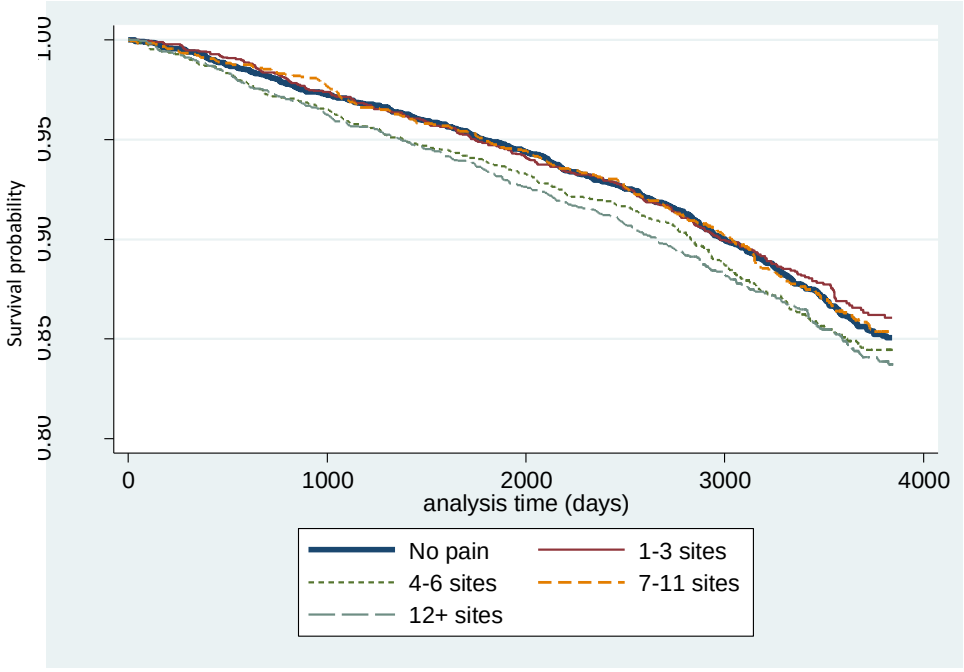


Figure 5.10 Survival probability over 10 years for number of pain sites; Kaplan Meier estimates in the NorStOP complete case sample (n=10953)

Mortality risk

There was a significant increased risk of mortality for participants with 12+ sites adjusted for age and sex only (MRR 1.18; 95%CI 1.02, 1.37). There was no trend of increased mortality risk with increased number of pain sites (Table 5.5).

5.7.7 Pain interference (NorStOP)

Tests of proportionality

For pain interference, the Schoenfeld tests for both the crude model (Model 1) (Chi^2=18.06, p=0.001), and the model adjusted for age, sex, education and adequacy of income (Model 3) (Chi^2=21.43, p=0.006) were statistically significant indicating the assumption of proportionality did not hold (Appendix V). To overcome the problems caused by non-proportionality it was necessary to split the analysis time into periods. In accordance with previous research that has shown increased mortality for people with pain in the first year of follow up (Jordan & Croft, 2010), the first time period ranged from 0-365 days (0-1 year) and the second time period was from the second year of follow up onwards >366 days (i.e. 2-10 years). The proportionality assumption was met for both of these time periods. In the first time period the Schoenfeld test for the crude model (Model 1) (Chi^2 0.66, p=0.416) and for Model 3 (Chi^2=10.88, p=0.209) were not statistically significant. In the second time period the Schoenfeld test for the Model 1 (Chi^2=6.80, p=0.147) and Model 3 (Chi^2=14.87, p=0.061) were also not statistically significant (Appendix V).

Table 5.5 Risk of all-cause mortality in the NorStOP complete case sample according to pain phenotype (n=10985)							
Pain phenotype	**N**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
No pain	3166	28813	412	14.30	Reference	Reference	Reference
Any pain	7819	71116	1072	15.07	1.05 (0.94, 1.18)	1.08 (0.96, 1.21)	1.06 (0.95, 1.19)
No pain	3166	28813	412	14.30	Reference	Reference	Reference
Pain but not ACR WP	5038	45709	714	15.62	1.09 (0.97, 1.23)	1.06 (0.94, 1.20)	1.05 (0.93, 1.19)
ACR WP	2749	25158	352	13.99	0.97 (0.85, 1.12)	1.10 (0.95, 1.26)	1.07 (0.92, 1.23)
No pain	3166	28813	412	14.30	Reference	Reference	Reference
Pain but not Manchester WP	6062	55194	827	14.98	1.05 (0.93, 1.18)	1.05 (0.93, 1.18)	1.03 (0.92, 1.16)
Manchester WP	1725	15673	239	15.25	1.06 (0.91, 1.25)	**1.19 (1.02, 1.40)**	1.16 (0.99, 1.36)
No sites	3166	28813	412	14.30	Reference	Reference	Reference
1-3 sites	1952	17843	245	13.73	0.96 (0.82, 1.12)	0.95 (0.81, 1.11)	0.95 (0.81, 1.11)
4-6 sites	1942	17559	276	15.72	1.10 (0.94, 1.28)	1.09 (0.94, 1.27)	1.08 (0.93, 1.26)
7-11 sites	1833	16836	241	14.31	1.00 (0.85, 1.17)	1.07 (0.92, 1.26)	1.05 (0.90, 1.24)
12+ sites	2060	18630	304	16.32	1.14 (0.98, 1.32)	**1.18 (1.02, 1.37)**	1.15 (0.99, 1.34)

MRR= Mortality Rate Ratio, 95% CI = 95% confidence interval
ACR = American College of Rheumatology, WP = Widespread pain
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education, adequacy of income
***per 1000 person-years**
MRRs in bold indicate significant associations

Survival probability over time

There was an observable trend between increased pain interference and decreased survival probability over time (Figure 5.11).

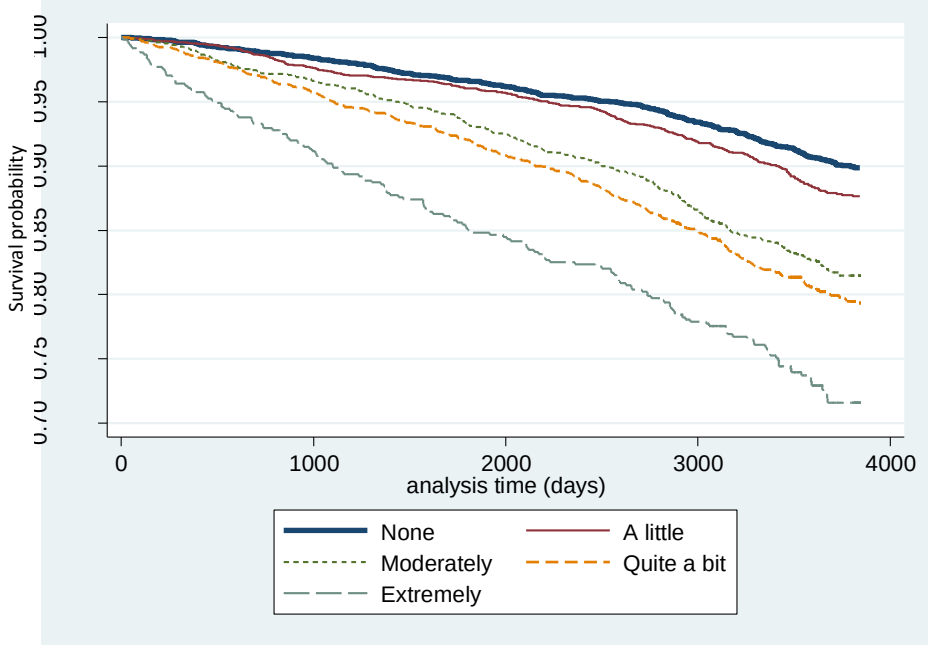


Figure 5.11 Survival probability over 10 years for pain interference; Kaplan Meier estimates in the NorStOP complete case sample (n=10985)

Mortality risk

The risk of mortality associated with pain interference was higher in first year of follow up than for the following 9 years (Tables 5.6 & 5.7). In the first year, 97 deaths occurred in the first 12 months; resulting in the power to detect a hazard ratio of 1.8 or above of 82%. There was no statistically significant increased risk of mortality for participants with "a little" or "moderate" pain interference in crude or adjusted models. There was a statistically significant increased risk of mortality for pain that interfered "quite a bit" in the crude model (Model 1: MRR 2.09; 95%CI 1.21, 3.59) and when adjusted for age and sex (Model 2: MRR 1.78; 95%CI 1.03, 3.08) but this attenuated and became non-

significant when adjusted for age, sex, education and adequacy of income (Model 3: MRR 1.54; 95%CI 0.88, 2.68). “Extreme” pain interference was statistically significantly associated with an increased risk of mortality in all models (Model 1: MRR 6.49; 95%CI 3.72, 11.33, Model 2: MRR 5.49; 95%CI 3.12, 9.65, Model 3: MRR 4.69; 95%CI 2.64, 8.34) (Table 5.6).

Table 5.7 displays the risk of all-cause mortality according to pain interference from 2 to 10 years of follow up. There was no increased risk of mortality for participants with “a little” pain interference in the crude or adjusted models. For participants who indicated “moderate” pain interference there was a statistically significant increased risk of mortality in the crude model only (Model 1: MRR 1.35; 95%CI 1.15, 1.58) which attenuated and became non-significant when adjusted for age and sex (Model 2: MRR 1.13; 95%CI 0.96, 1.33) and when adjusted for age, sex, education and adequacy of income (Model 3: MRR 1.13; 95%CI 0.96, 1.32). Compared to those with no pain participants reporting “quite a bit” or “extreme” pain interference had an increased risk of mortality in all models and were 38% and 88% respectively more likely to die after adjusting for all covariates in Model 3 (“quite a bit” Model 3: MRR 1.38; 95%CI 1.20, 1.59, “extremely” Model 3: MRR 1.88; 95%CI 1.54, 2.29) (Table 5.7).

Table 5.6 Risk of all-cause mortality in the NorStOP complete case sample according to pain interference in the first year of follow up (0-365 days)

Pain interference	N	Person years of follow up	Number of deaths	Mortality rate*	Model 1 MRR (95% CI)	Model 2 MRR (95% CI)	Model 3 MRR (95% CI)
No interference	4501	4489	27	5.01	Reference	Reference	Reference
A little	2316	2313	8	3.46	0.57 (0.26, 1.27)	0.61 (0.28, 1.35)	0.60 (0.27, 1.32)
Moderately	1562	1557	14	8.99	1.49 (0.78, 2.85)	1.31 (0.69, 2.50)	1.20 (0.63, 2.30)
Quite a bit	2004	1993	25	12.54	**2.09 (1.21, 3.59)**	**1.78 (1.03, 3.08)**	1.54 (0.88, 2.68)
Extremely	602	590	23	38.98	**6.49 (3.72, 11.33)**	**5.49 (3.12, 9.65)**	**4.69 (2.64, 8.34)**

MRR= Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education, adequacy of income
***per 1000 person-years**
MRRs in bold indicate significant associations

Table 5.7 Risk of all-cause mortality in the NorStOP complete case sample according to pain interference after the first year of follow up (365 to 3483 days)

Pain interference	N	Person years of follow up	Number of deaths	Mortality rate*	Model 1 MRR (95% CI)	Model 2 MRR (95% CI)	Model 3 MRR (95% CI)
No interference	4474	41269	472	11.44	Reference	Reference	Reference
A little	2308	21473	219	10.20	0.89 (0.76, 1.04)	0.94 (0.80, 1.10)	0.94 (0.80, 1.10)
Moderately	1548	14238	220	15.45	**1.35 (1.15, 1.58)**	1.13 (0.96, 1.33)	1.13 (0.96, 1.32)
Quite a bit	1979	17817	345	19.36	**1.70 (1.48, 1.95)**	**1.39 (1.21, 1.60)**	**1.38 (1.20, 1.59)**
Extremely	579	5078	131	25.80	**2.27 (1.87, 2.76)**	**1.89 (1.55, 2.30)**	**1.88 (1.54, 2.29)**

MRR= Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education, adequacy of income
***per 1000 person-years**
MRRs in bold indicate significant associations

5.7.8 Cause-specific mortality (ELSA only)

Hypothesis addressed:

The association between pain and cause-specific mortality is influenced by pain phenotype.

In ELSA cause of death was identified as cancer, cardiovascular disease, respiratory diseases, 'other' cause of death and 'unknown' cause of death. The results of the survival analyses for each of these causes are presented in this section.

Tests of proportionality

The tests of proportionality and associated plots are presented in Appendix V. The Schoenfeld plots and tests indicated there may be a problem with the proportionality assumption for:

1) Participants "often troubled" with pain and respiratory disease mortality

2) Participants with moderate pain and respiratory disease mortality

3) Moderate pain and cancer mortality

However, the global tests for Model 3 in both cases were non-significant indicating the proportionality assumption was reasonable in the fully adjusted models (Appendix V).

The reduction in the number of events when using cause specific deaths as the outcome resulted in reduced power to detect a relationship. The power to detect a HR 1.3 for cancer deaths = 0.5271, cardiovascular diseases = 0.4490, respiratory diseases = 0.2243, other cause of death = 0.2393. This problem would be compounded by splitting up the follow-up period to overcome any proportionality issues. The sample was therefore not

split and the results are presented for information but should be interpreted with caution.

C*ancer mortality*

1) *Often troubled with pain*

When compared to those not often troubled with pain, participants reporting they were "often troubled" with pain were not more likely to die from cancer over the follow up period (Model 3: MRR 1.08; 95%CI 0.83, 1.41) (Table 5.8).

2) *Severity of pain*

Participants with mild, moderate or severe pain were also not more likely to die from cancer over the follow-up period compared to those not often troubled with pain (Model 3: Mild: MRR 0.75; 95%CI 0.46, 1.23, moderate: MRR 1.19; 95%CI 0.87, 1.64, severe: MRR 1.32; 95%CI 0.82, 2.12) (Table 5.8).

Cardiovascular disease mortality

1) *Often troubled with pain*

Those "often troubled" with pain were more likely to die from cardiovascular disease (Model 1: MRR 1.48; 95%CI 1.12, 1.97) when compared to those not often troubled with pain. This increased risk was attenuated but remained statistically significant following adjustment for age and sex in Model 2 (MRR 1.39; 95%CI 1.05, 1.85), and attenuated further and was no longer statistically significant in Model 3 when additionally adjusted for education and wealth (MRR 1.30; 95%CI 0.98, 1.74) (Table 5.9).

Table 5.8 Risk of cancer mortality in the ELSA complete case sample according to pain phenotype (n=6324)							
Pain phenotype	**N**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
Not often troubled	4052	28048	148	5.28	Reference	Reference	Reference
Often troubled	2272	15414	91	5.90	1.12 (0.86, 1.46)	1.10 (0.84, 1.43)	1.08 (0.83, 1.41)
Not often troubled	4052	28048	148	5.28	Reference	Reference	Reference
Mild	680	4737	18	3.80	0.72 (0.44, 1.17)	0.75 (0.46, 1.23)	0.75 (0.46, 1.23)
Moderate	1183	7943	53	6.67	1.27 (0.93, 1.74)	1.20 (0.88, 1.65)	1.19 (0.87, 1.64)
Severe	409	2734	20	7.32	1.39 (0.87, 2.22)	1.34 (0.84, 2.13)	1.32 (0.82, 2.12)

MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education and wealth
***per 1000 person-years**
MRRs in bold indicate significant associations

Table 5.9 Risk of cardiovascular disease mortality in the ELSA complete case sample according to pain phenotype (n=6324)							
Pain phenotype	**N**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
Not often troubled	4052	28048	107	3.81	Reference	Reference	Reference
Often troubled	2272	15414	88	5.71	**1.48 (1.12, 1.97)**	**1.39 (1.05, 1.85)**	1.30 (0.98, 1.74)
Not often troubled	4052	28048	107	3.81	Reference	Reference	Reference
Mild	680	4737	16	3.38	0.88 (0.52, 1.50)	0.91 (0.54, 1.55)	0.97 (0.57, 1.63)
Moderate	1183	7943	52	6.55	**1.69 (1.21, 2.36)**	**1.51 (1.08, 2.11)**	1.37 (0.97, 1.92)
Severe	409	2734	20	7.32	**1.93 (1.19, 3.10)**	**1.82 (1.13, 2.95)**	1.61 (0.99, 2.61)

MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education and wealth
***per 1000 person-years**
MRRs in bold indicate significant associations

2) *Severity of pain*

There was a trend of increased risk of mortality due to cardiovascular disease with increased severity of pain. Those reporting mild pain did not have an increased risk of cardiovascular mortality (Model 1: MRR 0.88; 95%CI 0.52, 1.50, Model 2: MRR 0.91; 95%CI 0.54, 1.55, Model 3: MRR 0.97; 95%CI 0.57, 1.63). Moderate and severe pain were associated with an increased cardiovascular mortality risk which was robust to adjustment for age and sex (Model 2: moderate MRR 1.51; 95%CI 1.08, 2.11, severe MRR 1.93; 95%CI 1.19, 3.10) (Table 5.9). However, although an increased risk remained for moderate and severe pain, it was not statistically significant when adjusted for age, sex, education and wealth (Model 3: MRR 1.37; 95%CI 0.97, 1.92 and MRR 1.61; 95%CI 0.99, 2.61 respectively) (Table 5.9).

Respiratory disease mortality

1) *Often troubled with pain*

A significant increased risk of respiratory disease mortality was observed for those "often troubled" with pain (Model 1: MRR 1.92; 95%CI 1.25, 2.94) which remained statistically significant following adjustment for age, sex, education and wealth (Model 3: MRR 1.63; 95%CI 1.06, 2.51) (Table 5.10).

2) *Severity of pain*

Mild pain was not associated with increased respiratory disease mortality (Model 1: MRR 0.72; 95%CI 0.29, 1.83, Model 2: MRR 0.75; 95%CI 0.30, 1.90, Model 3: MRR 0.83; 95%CI 0.33, 2.10). Moderate and severe pain were associated with an increased risk of respiratory disease mortality which remained statistically significant following adjustment

for age, sex, education and wealth (Model 3: moderate pain: MRR 1.76; 95%CI 1.07, 2.89, severe pain: MRR 2.26; 95%CI 1.17, 4.34) (Table 5.10).

Other causes of mortality

1) *Often troubled with pain*

Table 5.11 displays the results of the survival analyses for known causes of death other than cancer, cardiovascular diseases or respiratory diseases. Being often troubled with pain was associated with other causes of mortality in the crude analysis only (Model 1: MRR 1.56; 95%CI 1.04, 2.36). The association between often troubled and mortality became non-significant following adjustment for confounders (Model 2: MRR 1.46; 95%CI 0.97, 2.22, Model 3: MRR 1.45; 95%CI 0.95, 2.19)

2) *Severity of pain*

Only moderate pain was associated with an increased risk of mortality for other known causes of death and this relationship was robust to adjustment for confounders (Model 1: MRR 2.03; 95%CI 1.27, 3.22, Model 2: MRR 1.81; 95%CI 1.13, 2.88, Model 3: (MRR 1.79; 95%CI 1.11, 2.88). Mild or severe pain was not associated with increased mortality risk from other known causes in any of the models (Table 5.11).

Unknown causes of mortality

1) *Often troubled with pain*

Participants “often troubled” with pain had a 41% increased risk of mortality from an unknown cause compared to those without pain after adjustment for age, sex, education and wealth (Model 3: MRR 1.41; 95%CI 1.03, 1.95) (Table 5.12).

2) Severity of pain

There was a trend of increasing risk of mortality from unknown causes with increasing severity of pain in crude analyses. Mild pain was again not associated with an increased mortality risk from unknown causes (Model 1: MRR 1.07; 95%CI 0.62, 1.85, Model 2: MRR 1.12; 95%CI 0.65, 1.94, Model 3: MRR 1.15; 95%CI 0.66, 1.99). Moderate and severe pain were associated with an increased risk of mortality from unknown causes in the crude analysis (Model 1: moderate pain: MRR 1.77; 95%CI 1.22, 2.56, severe pain: MRR 1.86; 95%CI 1.07, 3.22). For moderate pain the association remained significant when adjusted for age and sex (Model 2: MRR 1.66; 95%CI 1.14, 2.41) and when adjusted for age, sex, education and wealth (Model 3: MRR 1.52; 95%CI 1.04, 2.21). For severe pain this association attenuated and became non-significant when adjusted for age and sex (Model 2: MRR 1.72; 95%CI 0.99, 2.98) and age, sex, education and wealth (Model 3: MRR 1.50; 95%CI 0.86, 2.62) (Table 5.12).

Table 5.10 Risk of respiratory disease mortality in the ELSA complete case sample according to pain phenotype (n=6324)							
Pain phenotype	**N**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
Not often troubled	4052	28048	41	1.46	Reference	Reference	Reference
Often troubled	2272	15414	43	2.79	**1.92 (1.25, 2.94)**	**1.86 (1.21, 2.86)**	**1.63 (1.06, 2.51)**
Not often troubled	4052	28048	41	1.46	Reference	Reference	Reference
Mild	680	4737	5	1.06	0.72 (0.29, 1.83)	0.75 (0.30, 1.90)	0.83 (0.33, 2.10)
Moderate	1183	7943	26	3.27	**2.26 (1.38, 3.69)**	**2.11 (1.29, 3.46)**	**1.76 (1.07, 2.89)**
Severe	409	2734	12	4.39	**3.03 (1.59, 5.76)**	**2.99 (1.56, 5.70)**	**2.26 (1.17, 4.34)**

MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education and wealth
***per 1000 person-years**
MRRs in bold indicate significant associations

Table 5.11 Risk of other mortality in the ELSA complete case sample according to pain phenotype (n=6324)							
Pain phenotype	**N**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
Not often troubled	4052	28048	49	1.75	Reference	Reference	Reference
Often troubled	2272	15414	42	2.72	**1.56 (1.04, 2.36)**	1.46 (0.97, 2.22)	1.45 (0.95, 2.19)
Not often troubled	4052	28048	49	1.75	Reference	Reference	Reference
Mild	680	4737	6	1.27	0.72 (0.31, 1.69)	0.75 (0.32, 1.74)	0.75 (0.32, 1.76)
Moderate	1183	7943	28	3.53	**2.03 (1.27, 3.22)**	**1.81 (1.13, 2.88)**	**1.79 (1.11, 2.88)**
Severe	409	2734	8	2.93	1.68 (0.80, 3.55)	1.59 (0.75, 3.38)	1.57 (0.73, 3.34)

MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education and wealth
***per 1000 person-years**
MRRs in bold indicate significant associations

Table 5.12 Risk of unknown mortality in the ELSA complete case sample according to pain phenotype (n=6324)							
Pain phenotype	**N**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
Not often troubled	4052	28048	83	2.96	Reference	Reference	Reference
Often troubled	2272	15414	72	4.67	**1.57 (1.14, 2.15)**	**1.51 (1.10, 2.08)**	**1.41 (1.03, 1.95)**
Not often troubled	4052	28048	83	2.96	Reference	Reference	Reference
Mild	680	4737	15	3.17	1.07 (0.62, 1.85)	1.12 (0.65, 1.94)	1.15 (0.66, 1.99)
Moderate	1183	7943	42	5.29	**1.77 (1.22, 2.56)**	**1.66 (1.14, 2.41)**	**1.52 (1.04, 2.21)**
Severe	409	2734	15	5.49	**1.86 (1.07, 3.22)**	1.72 (0.99, 2.98)	1.50 (0.86, 2.62)

MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education and wealth
***per 1000 person-years**
MRRs in bold indicate significant associations

5.8 Discussion

5.8.1 Summary of results

The results of the survival analyses indicated the risk of mortality for people with pain was influenced by pain phenotype.

There was an increased risk of mortality for people who reported being “often troubled” with pain. This mortality risk increased with increased pain severity. Participants who were “often troubled” with pain had an increased risk of mortality from cardiovascular diseases, respiratory diseases, ‘other’ diseases and from unknown causes but not from cancer. For cardiovascular and respiratory disease mortality there was a trend of increased mortality risk with increased severity of pain.

There was no increased risk of mortality for people reporting “any pain” or with the majority of the definitions of the number of locations of pain (ACR WP, Manchester WP, number of pain sites) exceptions being Manchester WP criteria and 12 or more pain sites when adjusted for age and sex.

Pain interference was associated with an increased risk of mortality and this was higher in people reporting greater pain interference. The risk of mortality associated with pain interference was also greater in the first year of follow up. “Quite a bit” and “extreme” pain interference were associated with an increased risk of mortality in the first year of follow up and “moderate”, “quite a bit” and “extreme” pain interference were associated with increased mortality after the first year of follow up in crude models. The association between “extreme” pain interference and increased mortality was robust to adjustment for age, sex, education and adequacy of income in both time bands.

Overall these findings indicated that it was not simply the presence or number of locations of pain that was important for the relationship between pain and mortality but rather the impact of pain for the individual.

5.8.2 Methodological considerations

Although the findings of the current study indicate pain phenotype is important in the relationship between pain and mortality it was not possible to test all of the different pain phenotypes within one dataset. In order to test a range of phenotypes two datasets were used. Differences between the ELSA and NorStOP datasets may have influenced the pattern of findings:

Differences in sample structure

Differences in the structure of the study population between datasets may have influenced the observed relationships between pain phenotype and mortality risk. ELSA samples are generated with the intention of being representative of the English population of adults aged 50 years and over (i.e. representative at national level). In contrast the NorStOP dataset is sampled from a small number (n=8) of general practices in North Staffordshire and is less likely to be nationally representative. The geographical area covered by the NorStOP study is more deprived in terms of health, education and employment than England as a whole but with fewer barriers to housing and services (Wilkie, Blagojevic-Bucknall, Jordan, & Pransky, 2013). However, the age and sex structure of the participating NorStOP population is similar to that of North Staffordshire and to England and Wales (Thomas et al., 2007). Investigation of the age and sex distribution of the samples used for this study detailed in Chapter Four revealed that the

ELSA and NorStOP samples had similar structures to each other but the oldest age groups were under-represented in both datasets compared to national statistics. Other differences between the ELSA and NorStOP study samples may have influenced the observed relationships but these are difficult to quantify due to differences in the way variables were measured. Where measures were comparable i.e. for current smoking (ELSA =14.39%, NorStOP = 35.68%) and self-rated health rated as "excellent" (ELSA = 14.01%, NorStOP = 3.97%) these indicated the NorStOP sample may be a less healthy sample than the ELSA sample. Stronger associations between pain and mortality might therefore be expected in the NorStOP sample compared to the ELSA sample. However, in the current study this was not the case indicating other factors were influencing the relationship between pain and mortality.

Identification of vital status

The accuracy of the recording of vital status of participants was imperative to the current study. Misclassifications may result in an inaccurate representation of the true relationships between pain phenotype and mortality. Random-misclassification across pain phenotypes would lead to an underestimate of the true relationship between pain and mortality, whereas non-random misclassification could lead to an under or overestimate (Delgado-Rodríguez & Llorca, 2004). Vital status in the ELSA sample was determined using records from the Office of National Statistics whereas in NorStOP information was collated from two sources, the Exeter Patient registration system held at the local Primary Care Trust and through manual tracing of the NHS Summary Care Record Demographic system (see section 5.4.1). It is possible some misclassifications may have occurred; some deaths may have been missed or recorded in error, or the cause of

death may have been inaccurately documented. Although the recording of deaths is highly structured and standardised in developed countries, death certificates are sometimes not properly completed and discrepancies between the causes of death on death certificates compared to medical records have been observed (Johansson, Westerling, & Rosenberg, 2006). However, the United Kingdom is considered to have high quality death registration data (Mathers, Fat, Inoue, Rao, & Lopez, 2005) so any inaccuracies should be minimal. Despite differences in the sources of vital status information between the datasets, the proportion of deaths identified in the NorStOP and ELSA was similar (12.08% of the ELSA sample and 13.51% of the NorStOP sample died) over an approximately comparable follow-up period (8-10 years).

5.8.3 Comparison with other studies

The influence of pain phenotype

The current study examined mortality risk for novel pain phenotypes in addition to those previously examined in existing literature. The pain phenotypes tested in the NorStOP sample to measure the presence and location of pain were comparable to some phenotypes used in other studies (Macfarlane et al., 2001; McBeth et al., 2009), however the results were inconsistent with those studies. Macfarlane et al., 2001 used the ACR criteria to categorise widespread pain and found an increased risk of mortality for those meeting the criteria (MRR 1.31; 95%CI 1.05, 1.65, adjusted for age, sex and study location) (Macfarlane et al., 2001). Similarly McBeth et al., (2009) found an increased risk of mortality in participants meeting the ACR criteria for widespread pain (MRR 1.3; 95%CI 1.1, 1.5, adjusted for age, sex, practice, ethnic group and Townsend score of deprivation) (McBeth et al., 2009). However, in the current study, participants in the NorStOP sample

who met the ACR criteria for widespread pain did not have an increased risk of mortality compared to those with no pain (MRR 1.07; 95%CI 0.92, 1.23 adjusted for age, sex, education and adequacy of income).

Pain coding

Differences in the way widespread pain was coded between the current and previous studies may account for some of the differences in findings. In each of the above mentioned studies (including the current study), participants were asked to indicate the location of their pain on a blank body manikin so that pain according to ACR criteria for widespread pain (pain in the axial skeleton, on the right and left sides of the body and above and below the waist) could be determined. It is more practical and cost effective to use several raters to score completed pain drawings meaning the quality of the data is dependent on inter-rater reliability (Lacey, Lewis, Jordan, Jinks, & Sim, 2005). In a study carried out using the NorStOP dataset, the scoring of pain drawings by multiple raters was found to be highly reliable (agreement ranged from 82% to 100%) for all body areas excluding the back area of the head (Lacey et al., 2005). Other studies using the NorStOP dataset have reported a prevalence of Manchester WP of 12.5% (Thomas, Peat, et al., 2004), ACR WP 22.3% (McBeth, Lacey, & Wilkie, 2014) and 26.4 % (Wilkie, Tajar, & McBeth, 2013) which are similar to the figures reported in the current study; 25.03% met the criteria for widespread pain according to the ACR criteria, 15.70% met the Manchester criteria for widespread pain. Information regarding the way in which the drawings were scored in the Macfarlane et al., (2001) and the McBeth et al., (2009) studies was not available, but as detailed in Chapter Two, these studies were well conducted and the prevalence of widespread pain was consistent with other population

studies (Hunt et al., 1999; Wolfe, Ross, & Anderson, 1995). The Macfarlane et al., (2001) study reported the prevalence of widespread pain to be 15% (Macfarlane et al., 2001), the McBeth et al., 2009 study reported a prevalence of widespread pain of 16.9% (McBeth et al., 2009).

The higher prevalence of widespread pain (ACR and Manchester definitions) observed in NorStOP is likely due to the sample being restricted to adults aged 50 years and over. Good access to healthcare in the geographical area covered by NorStOP (North Staffordshire) despite its deprivation status (Wilkie, Blagojevic-Bucknall, Jordan, Lacey, & McBeth, 2013) may mean that despite the high prevalence of pain, these participants receive effective treatment for their pain which explains the lower mortality risk compared to the other studies. The Macfarlane et al., (2001) and the McBeth et al., (2009) studies were also both carried out in the Greater Manchester area of the UK which has one of the highest age standardised mortality rates in England and Wales (Office For National Statistics, 2012) which may also contribute to the observed differences in mortality between the studies.

Pain impact

The magnitude of the relationship observed in the ELSA dataset between "troubling" pain and all-cause mortality (MRR 1.29; 95% CI 1.12, 1.49) was comparable with the studies using a measure of widespread pain (see above) (Macfarlane et al., 2001; McBeth et al., 2009) and with those measuring chronic pain ((MRR 1.21; 95%CI 1.02, 1.44) (Sjøgren & Grønbæk, 2010) (Crude MRR 1.32; 95%CI 1.14, 1.54) (Torrance et al., 2010)). Consistent with the current study, Torrance and colleagues (2010) also reported a trend of increased mortality risk with greater pain severity (Torrance et al., 2010). The pain phenotypes in

ELSA dataset did not contain information regarding location or chronicity but participants were asked to indicate if they were “often troubled” with pain. It has been suggested this measure of pain may be an underrepresentation of the construct of pain as a positive response to the question “Are you often troubled with pain?” may only be forthcoming if pain is significant enough to be considered frequent (Reyes-Gibby et al., 2002). This way of assessing pain may therefore capture both the presence and some indication of the impact of pain. The NorStOP participants were asked if they had “any pain” and then asked to indicate the location. This is a validated approach to identifying the presence of pain and its location (Lacey et al., 2005; Margolis, Chibnall, & Tait, 1988; Weiner, Peterson, & Keefe, 1998) but does not necessarily capture the impact of pain. This may help to explain why the ELSA pain phenotypes were associated with mortality but the NorStOP phenotypes describing the presence and location of pain were not. In contrast, pain interference (a measure of pain impact) was associated with an increased risk of mortality in the NorStOP sample. The results of the current study indicate being “often troubled” with pain and pain interference are similar constructs and that the link between pain and mortality is dependent on pain impact rather than the presence or number of locations of pain.

Unexpected findings

The findings from the NorStOP sample are unexpected as an increasing number of pain sites has previously been reported to be associated with a reduction in overall health, sleep quality, psychological health and decreased function (Kamaleri et al., 2008) and with increased mortality (McBeth et al., 2009). However, the number of pain sites is not predictive of the rising impact of pain of daily life with age in this population (Thomas et

al., 2004). The use of a single item to capture pain interference has limitations. It has been suggested that older participants conflate reasons for 'interference with life' and do not distinguish pain as the main factor when answering the question (Thomas et al., 2007). An exploration of the relationship between the number of pain sites and pain interference variable used in this study is presented in Table 5.13. The highest proportion of deaths occurred for those reporting only 1-3 sites of pain but extreme pain interference (37.50%), although there were only a small number of participants in this category. There is some correlation between a greater number of pain sites and the extent of pain interference (Table 5.13). However in contrast to pain interference, the number of pain sites was not associated with increased mortality in this study.

Within the NorStOP questionnaire the question regarding pain interference was positioned in a general health section separate to the questions regarding the presence and location of pain; the pain interference question was asked early on in the survey (Section A, Part 1 (of 8), question 5). The question about the presence and location of pain was much later in the survey (Section B, Part 1) and was preceded by a statement saying the section was about any pains they may have or any problems with their joints. If the questions were positioned closer together in the survey, (i.e. the pain interference question followed the presence and location questions), responders may have focussed more on 'pain' as opposed to other reasons for interference with life when responding to the interference item. This may have reduced some of the contrasting relationships with mortality between the number of pain sites and pain interference in NorStOP. The findings from the current study indicate the measure of the number of pain sites is not a good proxy for the impact of pain in the NorStOP sample and that overall, in terms of the

Table 5.13 Cross tabulation of the number of pain sites and pain interference categories presenting the proportion of those who died in the NorStOP complete case sample (n= 10953) *						
	% who died (Number of deaths/N) per cell					
	No sites	**1-3 sites**	**4-6 sites**	**7-11 sites**	**12+ sites**	**Total**
No interference	13.01% (412/3166)	6.73% (46/683)	6.91% (26/376)	6.15% (12/195)	4.00% (3/75)	11.10% (499/4495)
A little	-	11.34% (81/714)	10.06% (72/716)	8.50% (48/565)	7.91% (25/316)	9.78% (226/2311)
Moderately	-	19.80% (59/298)	17.15% (71/414)	12.95% (57/440)	11.39% (46/404)	14.97% (233/1556)
Quite a bit	-	20.89% (47/225)	24.51% (87/355)	17.45% (89/510)	15.93% (144/904)	18.41% (367/1994)
Extremely	-	37.50% (12/32)	24.69% (20/81)	28.46% (35/123)	23.82% (86/361)	25.63% (153/597)
Total	13.01% (412/3166)	12.55% (245/1952)	14.21% (276/1942)	13.15% (241/1833)	14.76% (304/2060)	13.49% (1478/10953)
*excludes n=32 who indicated the presence of pain but did not indicate any pain sites on the pain manikin						

risk of mortality, the presence of pain is less important than the impact of that pain on the individual, irrespective of the amount.

Cause specific mortality

Previous studies have reported an increased risk of cancer mortality for people with pain (Macfarlane et al., 2001; McBeth et al., 2009). In the analysis of ELSA data in the current study there was no increased risk of cancer mortality for any of the pain phenotypes; rather the increased mortality risk from known causes was due to cardiovascular disease and respiratory disease mortality. Andersson (2009) reported an increased risk of cardiovascular disease mortality but no increased risk of cancer mortality for people with widespread pain (Andersson, 2009). Smith and colleagues (2003) also did not find an increased risk of mortality from cancer but did report increased mortality from respiratory diseases for people with chronic pain (Smith et al., 2003).

There was also an increased risk of mortality from 'other' and 'unknown' causes of death in the ELSA sample in the current study. This may include suicide, death from liver cirrhosis, cerebrovascular disease and accidents. These causes of death have been shown to be increased in patients with fibromyalgia (Dreyer et al., 2010; Wolfe et al., 2011). The 'unknown' category refers to participants that were known to have died but whose cause of death could not be determined. It is therefore possible these participants could fit into any of the categories of causes of death meaning the reported associations could be an underestimation of the true risk of those causes of death for people with pain. The lack of consistency or specificity of cause of death implies there is little evidence for any causal associations between pain and a specific cause of death (Hill, 1965); rather pain contributes to reduced survival more generally. The differences in the observed cause

specific deaths between studies may therefore be due to the different populations studied.

5.8.4 Strengths and limitations

Datasets

The current study was conducted using data obtained from two large population-based surveys with high response rates. It was possible to investigate the relationship between a number of different pain phenotypes and mortality. Although complete case analysis often results in a reduced sample size and reduced statistical power, the complete case samples in the current study had sufficient power to detect the expected effect sizes and the weighted analyses indicated the missing data did not introduce bias to the results. However, it was only possible to investigate cause-specific mortality in one of the data samples (ELSA) and the reduction in the number of deaths per cause meant these analyses were underpowered (described in section 5.7.8) and the results should be interpreted with caution.

As described in section 5.8.2, a potential limitation for the investigation of pain phenotype in the current study was the inability to test all of the phenotypes in the same data sample. However, the pattern of findings observed was contrary to what might have been expected given some of the observable differences between the datasets i.e. NorStOP participants were less healthy but those with pain did not have increased mortality. This suggests the use of two different samples was not responsible for the pattern of findings.

Mortality information

Only year of death information was available from the ELSA dataset. This has implications for the accuracy of the MRRs reported for the ELSA sample. For participants who died, the time in the study was calculated from their date of interview until 31st December in the year the participant was known to have died. The actual date of death may have been earlier meaning survival time was overestimated and mortality risk was underestimated for ELSA participants in the current study.

Pain phenotype

Although seven different phenotypes (and their sub-categories) of pain were examined in the current study, it was not possible to determine pain that was chronic (i.e. lasting for three months or more) in either the ELSA or NorStOP datasets. Pain was measured at one point in time only and it is possible participants may have been misclassified or changed pain state over the follow-up period. This would result in an inaccurate representation of the relationship between pain and mortality (either an under or over-estimation) but the number of misclassifications of pain state is likely to be small, resulting in minimal effect on the overall findings.

5.8.5 Implications for further research

The findings from the survival analyses in the current study demonstrated an increased risk of mortality for people who had pain that impacted on their life. The presence of pain alone or an increased number of sites of pain was not associated with an increased risk of mortality. An investigation of potential mechanisms for a relationship, which would establish *how* pain impacts on a person's life, may identify potential targets to prevent

mortality. As described in Chapter Two, previous studies of the relationship between pain and mortality considered lifestyle factors and psychological factors as potential confounders. Following on from this chapter, this thesis further adds to the existing body of knowledge by investigating the specific role of lifestyle, health, social and psychological factors by treating them as potential mediators or moderators of the relationship between pain and mortality (presented in Chapter Six). A better understanding of the mechanism between pain and mortality could guide strategies to reduce the impact of pain and prevent mortality by identifying targets for interventions.

5.9 Key messages

- Pain phenotype influenced the strength of association between pain and mortality
- Pain impact is key to understanding the relationship between pain and mortality
- Pain considered to be “troubling” was associated with mortality from cardiovascular disease, respiratory disease, other known causes and unknown causes of death
- An investigation of potential mechanisms of a relationship between pain and mortality is warranted

Chapter Six. Mechanisms of association between pain and mortality

6.1 Introduction

Mortality risk was greater in people who had pain which impacted on their life (Chapter Five) highlighting a need to identify how the increased risk of mortality in those with pain occurred. In previous studies of pain and mortality (described in Chapters One and Two) covariates (e.g. physical activity, smoking etc.) were included in the analysis as confounders and simply adjusted for in the survival models. No previous studies have examined the roles these factors might play. This chapter presents novel analyses which tested if lifestyle, health, social and psychological factors were mediators of the relationship (i.e. lay on a pathway) between pain and mortality. In addition, as the pathways between pain and mortality may differ in different subgroups, potential moderators of the pathways from pain to mortality were tested to investigate in whom the relationships existed. The specific hypotheses are presented in section 6.2. Understanding how the relationship between pain and mortality may work has important implications for the management of pain by providing information on where to target interventions.

6.2 Aims

The aims of the analysis presented in this chapter were to:

1. Identify mediators of the association between pain and mortality
2. Examine the potential moderating effects of sex and comorbidity on the proposed pathways from pain to mortality

The following hypotheses were tested:

Hypothesis 1

The relationship between pain and mortality was mediated by lifestyle, health, social and psychological factors.

Hypothesis 2

The pathways from pain to mortality were different in males and females

Hypothesis 3

The pathways from pain to mortality were different in those with existing comorbidity compared to those without

6.3 Methods

6.3.1 Mediation

The aim of mediation analysis is to test *how* a predictor exerts influence on an outcome. Hypothesised relationships between variables can be represented using path diagrams which indicate the direction of influence in relationships between variables (Figure 6.1). Links from causes to effects are represented by single headed arrows and directed (or causal) paths can be followed through a sequence of single-headed arrows (Greenland et al., 1999).

Mediation analysis involves the estimation of two effects: The direct effect of an exposure on an outcome (c') and the indirect effect (ab) which acts through an intervening variable that is hypothesised to be on a causal pathway from the exposure to the outcome (Rochon, du Bois, & Lange, 2014). The sum of these two effects equals the total effect (Rochon et al., 2014) (Figure 6.1).

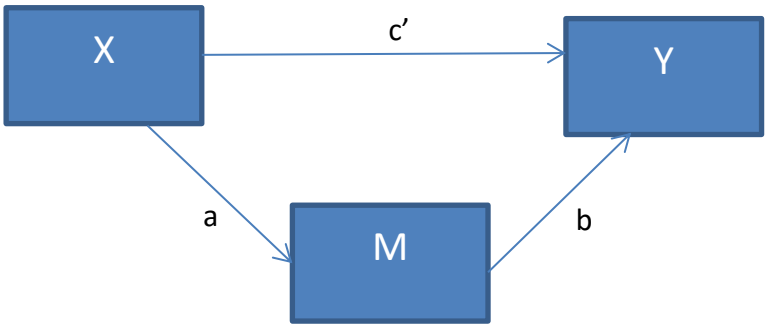


Figure 6.1 Simple mediation model

X= exposure, Y = outcome, M= mediator, c' = direct effect, a = effect of exposure on the mediator, b = effect of the mediator on the outcome, ab = the indirect effect, ab + c' = total effect (c)

A mediating variable may explain part of an observed effect where a predictor variable (X) and outcome (Y) are associated and the mediator variable (M) accounts for at least some of that association, in other words there are direct (c') and indirect effects (ab) of the predictor on the outcome (Figure 6.1) (Hayes, 2009). Alternatively, it may be that X only influences Y indirectly through the mediator(s) M (i.e. there is an indirect effect only) (Hayes, 2009) (Figure 6.1).

The terms mediating effect and indirect effect are often used interchangeably (Hayes, 2007) and both terms are used in this thesis. The term mediating effect is used when there is an effect to be mediated (i.e. in the presence of a statistically significant total effect). The term indirect effect is used where there is a statistically significant indirect effect only (Hayes, 2009) (i.e. the predictor influences the outcome only through the intervening variable). In both instances the mediating/indirect effect may also be described as a 'pathway' from predictor to outcome via the intervening variable (Emsley, Dunn, & White, 2010; Hayes, 2009; Kline, 2015; Rucker, Preacher, Tormala, & Petty, 2011). To help answer questions about causal relationships the proposed pathways in mediation analysis have a temporal element; the mediator is assumed to be a

consequence of the predictor and a precursor to the outcome (Hayes, 2013). For example, pain may lead to physical inactivity which in turn leads to subsequent mortality. A change in the mediator (i.e. through a health intervention to increase physical activity) would subsequently result in a change in the outcome (i.e. reduce the risk of mortality).

Investigation of whether a third factor "mediates" the link between an exposure and outcome enhances the understanding of how and why the relationship exists by providing insight into potential causal mechanisms and (when combined with moderation analysis) the circumstances under which interventions will work (Hafeman & Schwartz, 2009; Hayes, 2013).

6.3.2 Mediation analysis

There are traditionally two approaches to mediation analysis. The first is the 'product method' initially proposed by Baron and Kenny (1986) whereby the indirect effect is determined from the product of the coefficient for the exposure in the model for the mediator (path a, Figure 6.1) and the coefficient for the mediator in the model for the outcome (path b, Figure 6.1) (ab = indirect effect) (Baron & Kenny, 1986). The second is the 'difference method' where a model is fitted with and without the mediating variable and the difference in the coefficients for the exposure is taken to be the measure of the mediated effect (Judd & Kenny, 1981). Where the variables are continuous these results are equivalent but with categorical and binary data the two methods diverge (Preacher, 2015) and an alternative approach may be more appropriate. Different techniques for undertaking mediation analysis are described below.

Structural equation modelling (SEM) is commonly used to analyse mediation between an exposure and an outcome (Streiner, 2005). SEM estimates the strength of relationships

between variables using a combination of confirmatory factor analysis and path analysis to form a model which can be tested statistically (Streiner, 2005). Variables in structural equation models can be both measured (observed) and latent. Latent variables are not directly observed, rather they are hypothetical constructs represented by a number of observed variables (MacCallum & Austin, 2000). Direct (c') and indirect relationships (ab) (see Figure 6.1) between these variables can be estimated (Hays, Revicki, & Coyne, 2005). Path analysis techniques work in a similar way but use only observed variables in the model. Path analysis is undertaken when it is the observed variable that is of primary interest or if there are too few observed variables to construct a latent variable (MacCallum & Austin, 2000).

Procedures to estimate direct and indirect effects are influenced by different types of data (binary, continuous, categorical, survival etc.) As the outcome (dead or alive) in this study was binary it was not possible to use traditional structural equation modelling techniques in order to conduct the analysis as these assume continuous normally distributed data (MacCallum & Austin, 2000). It was therefore necessary to investigate different methods to find the most appropriate. The following approaches were considered:

Karlson Holm Breen (KHB)

The Karlson-Holm-Breen (KHB) method was specifically designed for use in Stata to extend the decomposition features of linear models to binary non-linear probability models (Karlson, Holm, & Breen, 2010). The KHB method decomposes the total effect of an exposure on an outcome in a logistic model into direct and indirect effects. It was

developed for use with binary models, but can decompose effects for discrete and continuous variables. It also provides statistical tests by which to assess the models.

In linear models decomposing direct and indirect effects involves comparing a 'reduced model' with no mediator present to a 'full model' which includes the mediating variable. The difference between the two models equates to the direct effect (i.e. the difference method, see section 6.3.1). However, in nonlinear models the estimated coefficients are not comparable between models due to a rescaling as a result of joint identification of the coefficients and error variances (Karlson & Holm, 2011). In linear models the regression coefficients and error variances for the direct and indirect effect are separately identified. In non-linear models the coefficients in the model are a ratio of the true regression coefficient divided by a scale parameter dependent on the error standard deviation (Karlson et al., 2010) resulting in coefficients for the direct and indirect effects which, when summed, do not equal the total effect. The KHB method overcomes this problem by substituting the mediators by the residuals of the mediators from a regression of those mediators on the key variables of interest. This then allows comparison of the full model to the reduced model as in linear models and a calculation of the proportion of the total effect that is explained by the indirect effect (Karlson & Holm, 2011). However, this method was not designed for use in survival analysis and does not allow for the influence of time in the study.

Generalised Structural Equation Modelling (GSEM)

Generalised linear modelling (GLM) allows for non-linear functional forms and non-normal response distributions and unifies disparate statistical techniques such as linear regression, logistic regression and Poisson regression under a single framework

(Tomarken & Waller, 2005). This framework is utilised by GSEM in Stata version 13 and allows for different types of response processes including continuous, censored, grouped, ordinal and dichotomous and automatically accommodates missing data (Rabe-Hesketh, Skrondal, & Pickles, 2004). GSEM in Stata 13 is a powerful package that enables very complex data analysis of multilevel models and allows for the inclusion of both measured and latent variables. However, it is in the early stages of development and at present there are a number of limitations. Firstly, whilst it was possible to produce exponentiated coefficients in the form of odds ratios, these can be difficult to interpret due to the joint identification issue described above (where the direct and indirect effects do not sum to equal the total effect) and as with the KHB method, the output is not comparable to the hazard ratios produced when using survival analysis. GSEM has not yet been extended to include syntax which enables mediation analysis to be undertaken with survival data. GSEM also does not currently calculate model fit statistics and does not have the multiple group comparison techniques offered by SEM so it was deemed there would be no advantages of using this package for this study.

Mediation analysis within survival analysis

The major limitation of the techniques described above is that they share an inability to account for time, and as a consequence the results from these approaches are not comparable to those from survival analysis.

Within the proportional hazards model neither the 'product method' nor the 'difference method' have a clear causal interpretation as a measure of effect (Vanderweele, 2012). In response to these limitations Lange and colleagues (2012) suggested a unified model which can be used for any type of outcome and any type of mediator. It does not work by

combining parameter estimates from standard models for the mediator and outcome, rather the approach is based on the counterfactual framework and directly models the direct and indirect effects of interest.

Counterfactual framework

In time-to-event analysis, such as a Cox's proportional hazards model with a binary exposure and mediator, Lange and colleagues (2012) showed that a weighted Cox regression produces unbiased estimates for the direct and indirect effects (Lange, Vansteelandt, & Bekaert, 2012). Within the counterfactual framework each participant is observed under one set of circumstances but consideration is also given to what would have happened to that participant under counterfactual circumstances (those that did not occur) (Robins & Greenland, 1992). This involves replication of analyses whereby, in the first instance the exposure takes the original value and in the second replication it takes the opposite or counterfactual value. Weights are derived from logistic regression of the binary mediator on the exposure and baseline confounders as follows:

$$W_i^c = \frac{P(M = M_i \,|A = A_i^*, C = C_i)}{P(M = M_i \,|A = A_i, C = C_i)}.$$

Where A is the observed exposure of interest; M is the mediator and C, a set of baseline confounders.
* represents the counterfactual value(s)

Where the assumptions of proportional hazards and non-informative censoring are met, the weighted Cox regression model will give hazard ratios which are estimates for the direct and indirect effects. The product of these two hazard ratios provides the hazard ratio for the total effect. This is the approach used by Rochon et al., (2014) in their development of code for mediation analysis for the statistical package R. Standard error and confidence intervals are calculated using bootstrapping (Rochon et al., 2014).

Bootstrapping

Bootstrapping is a resampling procedure which is used to determine the accuracy of a parameter through the calculation of confidence intervals (Preacher & Hayes, 2008a). The process involves taking a new sample size from the original sample and estimating the values of the indirect effect (Preacher & Hayes, 2008a). An individual case may be selected as part of a bootstrap sample any number of times; referred to as bootstrapping with replacement (cases are 'replaced' into the original sample each time) (Preacher & Hayes, 2008a). This resampling process is repeated *k* number of times. The distribution of the *k* values of the indirect effects generated serves as a non-parametric estimation of that distribution, the mean can be considered as a point estimate of the indirect effect, the standard deviation as a the standard error of the sampling distribution and confidence intervals are derived by sorting the *k* values of the indirect effect from low to high (Preacher & Hayes, 2008b). For the calculation of confidence intervals it is recommended the resampling procedure is undertaken at least 1000 times (Efron & Tibshirani, 1986; Preacher & Hayes, 2008b). A disadvantage of using bootstrapping is that it can be time consuming to carry out the ideal number of replications. This was one limitation of this study. Due to time constraints only 100 replications were undertaken for each model. However, for the model demonstrating the most uncertainty (widest confidence interval) the analysis was re-run using 1000 replications which resulted in minimal changes to the confidence intervals.[1]

[1] This was the model for females in ELSA with symptoms preventing walking as the mediating variable. In the analysis using 100 bootstrap replications the results were: Direct effect: HR 0.87; 95%CI 0.69, 1.15; indirect effect: HR 1.43; 95%CI 1.26, 1.57: total effect: HR 1.24; 95%CI 0.98, 1.55. In the model using 1000 replications the results were: Direct effect: HR 0.87; 95%CI 0.68, 1.10; indirect effect: HR 1.43; 95%CI 1.27, 1.61: total effect: HR 1.24; 95%CI 0.99, 1.54).

6.3.3 Measurement of the proposed mediators in the ELSA and NorStOP datasets

There are a number of factors that are potential mediators of the relationship between pain and mortality; those examined in this study were chosen as they have been shown to be associated with both pain and mortality, and theoretically could occur as a consequence of pain and lead to mortality (described in section 2.8). Whilst the analyses in the current study were restricted by the use of secondary data and the information available, the ELSA and NorStOP datasets provided data on a wide range of factors that could be investigated. Variables from lifestyle, health, social and psychological domains were tested as potential mediating variables in the relationship between pain and mortality. The factors are grouped into the above domains as defined in Chapter Two (Section 2.8) in order to structure the presentation of this chapter.

Tables 6.1 to 6.4 summarise the proposed mediators in the ELSA and NorStOP datasets. The statistical technique used to undertake the mediation analysis in this study (described in section 6.3.2) required the mediators to be binary variables. The tables therefore include the following information:

a) The method used to measure each mediator
b) The range of scores or included categories (where appropriate)
c) The way in which the variables were dichotomised

Further information about the measurement of each variable, including detail of scales and psychometric properties (where appropriate) is presented in Appendix VII.

Table 6.1 Measures of the proposed mediating lifestyle factors in the ELSA and NorStOP datasets				
Proposed mediator	**Dataset**	**Measure**	**Categories/ Range**	**Dichotomy**
Physical activity	ELSA	Mild, moderate or vigorous activity	More than once a week Once a week One to three times a month Hardly ever	No/mild activity at least once a week (reference) Moderate/vigorous activity at least once a week
	NorStOP	Single item: Frequency go out	All days Most days Some days Few days No days	Few / no days (reference) All/most/some days
		Single item: Frequency walk for 10 minutes	Daily Every other day Twice per week Less than twice per week Not at all	Less than weekly (reference) Weekly or more
Smoking	ELSA	Single item: Smoker status	Never Used to be an occasional smoker Regular or frequent smoker Current smoker	Never and past smoker (reference) Current smoker
	NorStOP	Single item: Smoker status	“never smoked” “previously smoked” “currently smoking”	Never/previous smoker (reference) Current smoker

Alcohol	ELSA	Single item: Frequency of alcohol consumption over the last 12 months	Not at all Once or twice a year Once every couple of months Once or twice a month Once or twice a week Three or four times a week Five or six days a week Almost every day	Less than weekly (reference) Weekly or more
	NorStOP	Single item: On average how often do you drink alcohol?	Daily or most days Once or twice a week Once or twice a month Once or twice a year Never	Less than weekly (reference) Weekly or more
Obesity	NorStOP	BMI = weight (kg)/[height(m)]^2	Underweight (< 18.5 kg/m^2) Normal (18.5-24.9 kg/m^2) Overweight (25.0-29.9 kg/m^2) Obese (≥30 kg/ m^2)	Not obese (reference) Obese
Sleep	NorStOP	JSQ: Number of days in the past month: 1) Trouble falling asleep 2) Wake in the night 3) Trouble staying asleep 4) Wake up unrefreshed	 Not at all Some nights Most nights	None/some (reference) Most nights
JSQ = Jenkins sleep questionnaire (Jenkins, Stanton, Niemcryk, & Rose, 1988).				

Table 6.2 Measures of the proposed mediating health factors in the ELSA and NorStOP datasets				
Proposed mediator	**Dataset**	**Measure**	**Categories/ Range**	**Dichotomy**
Self-reported health	ELSA	Single item: Health rating	Excellent Very good Good Fair Poor	Fair/Poor (reference) Good/Very good/Excellent
	NorStOP	Single item (MOS-SF12)	Excellent Very good Good Fair Poor	Fair/Poor (reference) Good/Very good/Excellent
Functional limitation	ELSA	Difficulties with ADL and IADL	0-13	No difficulties (reference) Any difficulties
	NorStOP	MOS SF-36 10 item physical functioning scale	0-100	<median (low function) (reference) >median (high function)

Symptoms preventing walking ¼ mile	ELSA	Items combined to form a single item	Chest pain Fatigue/too tired Shortness of breath Tremor Pain in leg or foot Swelling in leg or foot Incontinence Seeing difficulty Hearing difficulty Confusion Difficulty concentrating Memory problems Unsteady on feet or balance problems Lightheaded or dizziness Fear of falling Anxiety or fear Other problem or symptom	No difficulties (reference) Any difficulties
Allostatic load (AL)	ELSA	Biomarkers: 1) Systolic blood pressure 2) Diastolic blood pressure 3) Mean arterial pressure 4) Resting pulse rate 5) Fibrinogen 6) High density lipid cholesterol (HDL) 7) Low density lipid cholesterol (LDL) 8) C-reactive protein (CRP) 9) Glycosylated haemoglobin (HBA1C) 10) Waist/hip ratio	0-10 (Participants were allocated a score of 1 when their score was above the highest 25th percentile for nine of the measures and below the 75th percentile for HDL)	<median (low AL) (Reference) >median (High AL)

Frailty	ELSA	Frailty criteria (Fried et al., 2001). Presence of 3 or more of the following: Weight loss Low grip strength Low walking speed Low physical activity levels Exhaustion	 loss of ≥10% body weight since Wave 0 survey or BMI<18.5 in the lowest 20% of the distribution of scores, adjusted for age and sex, for maximum grip strength tested using a dynamometer in the lowest 20% of the distribution for time taken to walk 8 feet at “usual” pace in the lowest sex specific 20% distribution for activity level (derived from the 3 questions about activity levels) Positive response to 2 CES-D questions (‘felt everything was an effort’ and ‘could not get going’ in the last week).	Not frail (reference) Frail
MOS SF-12 = Medical Outcomes Study Short Form 12 (Ware et al., 1995) ADL = Activities of Daily Living IADL = Instrumental Activities of Daily Living MOS SF-36 = Medical Outcomes Study Short Form 36, 10 item physical functioning scale (Ware & Sherbourne, 1992) CES-D = Centre for Epidemiological Studies Depression Scale (Radloff, 1977)				

Table 6.3 Measures of the proposed mediating social factors in the ELSA and NorStOP datasets				
Proposed mediator	**Dataset**	**Measure**	**Categories/ Range**	**Dichotomy**
Social group membership	ELSA	Current membership or participation in: 1) Political party, trade union or environmental group 2) Tenants groups, resident groups or neighbourhood watch 3) Church or other religious groups 4) Charitable associations 5) Education, art or music groups or evening classes 6) Social club 7) Sports club, gym or exercise classes 8) Any other organisations, clubs or societies	0-8	<median (low) (reference) >median (high)
Social participation restriction	NorStOP	KAP	0-11	No restriction (0) (reference) Any restriction (1-11)
Volunteer work	ELSA	Frequency of volunteer work	Twice a month or more About once a month Every few months Once or twice a year Less than once a year Never	None (reference) Any
KAP = Keele Assessment of Participation (Wilkie, Peat, Thomas, Hooper, & Croft, 2005)				

Table 6.4 Measures of the proposed mediating psychological factors in the ELSA and NorStOP datasets				
Proposed mediator	**Dataset**	**Measure**	**Categories/Range**	**Dichotomy**
Quality of life	ELSA	CASP-19: Control (e.g. 'I feel free to plan for the future') (4 items) Autonomy (e.g. 'I feel that I can please myself what I do') (5 items) Self-realisation (e.g. I feel that life is full of opportunities') (5 items) Pleasure (e.g. 'I enjoy the things that I do') (5 items)	Often Sometimes Not often Never (Scored 3-0 unless negatively worded where reversed)	< median (low) (reference) >median (high)
Anxiety	NorStOP	HADS	0-21 Non cases 0-7 Possible cases 8-10 Probable cases 11-21	Non cases (reference) Possible/probable cases
Depression	ELSA	Eight item version of CES-D	0-8	No depression (0-3) (reference) Possible case (4-8)
	NorStOP	HADS	0-21 Non cases 0-7 Possible cases 8-10 Probable cases 11-21	Non cases (reference) Possible/probable cases
Cognitive impairment	ELSA	Memory test. Immediate and delayed recall of 10 words	0-20	< median (low) (reference) >median (high)
	NorStOP	10 item Cognitive and Alertness Behaviour Scale from the FLP	0-100%	0 (no cognitive impairment) (reference) >0 Impairment

Perceived control over health	NorStOP	Single item from the IPQ-R: 'There is a lot I can do to control my health'	No Yes	No (reference) Yes

CASP-19 = Control, Autonomy Self-realisation, Pleasure scale (Hyde et al., 2003)
CES-D = Centre for Epidemiological Studies Depression Scale (Radloff, 1977)
FLP = Functional Limitations Profile (British version of the Sickness Impact Profile) (Bergner, Bobbitt, Carter, & Gilson, 1981)
IPQ-R = Illness Perceptions Questionnaire (Moss-Morris et al., 2002)

6.3.4 Mediation analysis within the ELSA and NorStOP samples

Predictor variables

The pain phenotypes used in this analysis were; from ELSA the variable "often troubled with pain/not often troubled with pain" and from NorStOP the "any pain/no pain" variable. This was to ensure the dichotomous predictor variables were comparing a "pain" group to a "no pain" group and that the analyses included the highest number of participants as possible to maximise the power to detect effects where they existed. It would have been preferable to dichotomise the pain interference ("pain interference/no pain interference") variable to use as the predictor variable as pain interference was associated with increased mortality. However, the risk of mortality was not proportional across the whole follow-up period (see section 5.7.7) so it was impractical to use this variable as the predictor in the mediation analysis. Although the report of "any pain" was not associated with mortality it was possible indirect pathways from pain to mortality would still exist (Hayes, 2009).

Available sample sizes for mediation analysis

Mediation analysis was carried out using the technique developed by Rochon et al., (2014) described in section 6.3.2 using R. The R code used to perform the analysis is presented in Appendix VIII. Analysis was conducted on all participants with complete data at baseline (ELSA n=6234, NorStOP n=10985). The potential mediating role of allostatic load and frailty were examined in separate "allostatic load" (n=4627) and "frailty" (n=4375) samples from the ELSA dataset.

Procedure

First, associations between the predictor and each mediating variable were examined using logistic regression to explain the direction of any mediating effect (i.e. a negative association (odds ratio less than 1) between pain and greater physical activity means the hazard ratio (above 1) of the indirect effect refers to an increased risk of mortality as a result of pain and lower levels of physical inactivity). The association between the mediator and outcome is not reported due to the use of the counterfactual framework to calculate the indirect effect directly (described in section 6.3.2) i.e. without combining parameter estimates from standard models for the mediator and outcome. All associations between pain phenotype and mediator variable are presented as odds ratios (OR) with 95% confidence intervals. All analyses were adjusted for putative confounders (age, sex education and wealth (ELSA)/ adequacy of income (NorStOP)). Results of the mediation analyses are presented as hazard ratios (HR) for the direct, indirect and total effects with associated 95% confidence intervals.

6.3.5 Moderation

In addition to examining the pathways from pain to mortality, the current study also tested the effects of potential moderators on these relationships. Moderation occurs when the effect of a predictor (X) on an outcome (Y) varies as a function of a third (moderating) variable; also known as an effect modifier (Figure 6.2) (Hayes, 2009; Rothman, 1986; Ryu, West, & Sousa, 2009). For example, in this thesis sex was proposed as a moderator of the relationship between pain and mortality. If the relationship between pain and mortality was significantly different in females compared to males, sex would be considered as an effect modifier or moderator of the relationship between pain

and mortality. Effect modification contributes to a more detailed description of the effect under investigation by determining in whom relationships exist (Rothman, 1986).

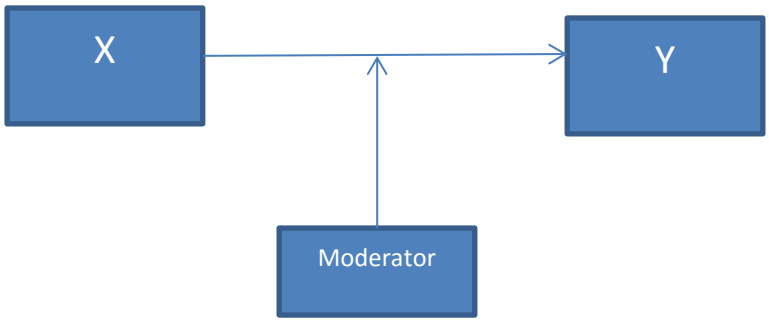


Figure 6.2 Simple moderation model

X=predictor, Y = outcome

6.3.6 Moderation analysis

The most common statistical way to test for moderation is to include an interaction term which is the product of X (predictor) and M (moderator) in a model of Y (outcome) (Hayes, 2013). For example, in a model which includes X (pain) and M (sex) as predictors of Y (mortality), if the product of X x M (pain x sex) is also entered into the model and is significantly associated with Y (mortality) then the relationship between X (pain) and Y (mortality) is moderated by M (sex).

An alternative approach to investigating moderating effects is sub-group analysis and is described in section 6.3.7.

6.3.7 Combining mediation and moderation

Combining mediation and moderation analyses allows the assessment of both how and in whom a relationship exists (Figure 6.3). Moderated mediation is said to occur when the strength of an indirect effect is dependent on the level of another variable, the moderator

(Hayes, 2007). This could be the result of an interaction between the predictor (X) and the moderator (as in the example in section 6.3.6) or the mediator and the moderator (Hayes, 2013). For example the moderator (sex) might interact with a proposed mediator (alcohol consumption) leading to a difference in the magnitude of an indirect effect from pain to mortality via alcohol consumption between males and females. The method of mediation analysis used in this study (described in section 6.3.2) is an emerging technique in which it was not possible to include interaction terms. Moderation was therefore assessed using sub-group analysis[2].

Sub-group analysis involves dividing the sample into groups according to levels of the moderator variable (e.g. males and females) and observing the relationship of interest in each of those groups (Edwards & Lambert, 2007). This approach is not generally recommended as a test of moderation as a statistical significance in one group but not in another does not imply a significant difference between the two groups. Similarly, significance or non-significance in both groups does not imply there is no difference between them (Hayes, 2013). However, statistical significance is linked to hypothesis testing and decision making but provides little information about the size of an effect and therefore can be misleading (Rothman, 1986). The calculation of confidence intervals around a point estimate (as has been done in this study), whilst also giving an indication of statistical significance (if the interval does not contain the null value e.g. a hazard ratio of 1) also provides an estimate of magnitude of the effect and the precision of the estimate (Rothman, 1986). Where confidence intervals are calculated in sub group

[2] Interaction terms were included in the adjusted survival models presented in Chapter 5 to test for a significant interaction between pain phenotype and sex and between pain phenotype and comorbidity and the results are reported for information in Appendix VI.

analysis, if the confidence intervals for each group do not overlap, the difference between the groups is statistically significant (Bland & Peacock, 2002). Sub-group analysis was therefore used in this study to assess the possible moderating effects of sex and comorbidity on any mediated relationships between pain and mortality.

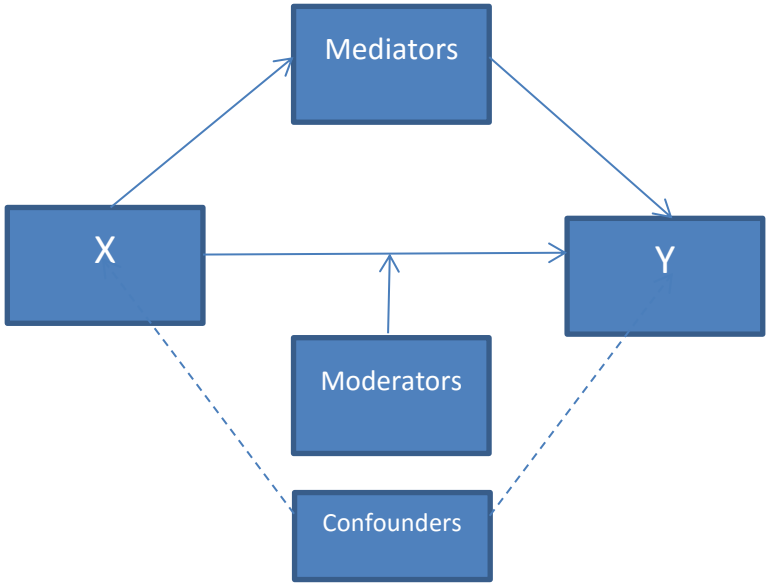


Figure 6.3 Moderation and mediation model

X= exposure, Y = outcome

6.3.8 Measurement of the proposed moderators in the ELSA and NorStOP datasets

Sex and the presence of comorbidity were hypothesised to moderate the pathways between pain and mortality (see section 2.9). The method used to measure sex in each of the datasets is described in Section 5.4. The method of measurement for comorbidity is described below.

Co-morbidity

In ELSA, participants were asked to indicate if a doctor had ever told them they had or have a number of chronic conditions. Participants were asked to choose from a list of 22 possible conditions and could indicate other conditions that were not on the list. Responses were recoded into dichotomous variables (present or absent) for cardiovascular disease (present if participants reported having or having had high blood pressure or hypertension, angina, heart attack (including myocardial infarction or coronary thrombosis), congestive heart failure, a heart murmur, abnormal heart rhythm, diabetes or high blood sugar, a stroke or any other heart trouble), respiratory diseases (participants report having or having had chronic lung disease (i.e. chronic bronchitis, emphysema or asthma), cancer or malignant tumour (excluding minor skin cancers)) or other comorbidity (arthritis (including osteoarthritis and rheumatism), osteoporosis, Parkinson's disease, any emotional or psychiatric problems, Alzheimer's disease or dementia) (NatCen Social Research, 2014b). To examine for possible moderation by comorbidity, the sample was divided into two groups; those who did not indicate any morbidities (a score of 0) and those who indicated any of the listed conditions (score >0).

In NorStOP, participants were asked to report the presence of three common chronic health conditions (chest problems, heart problems, diabetes), two impairments most commonly associated with disability (deafness, problems with eyesight) and seven other impairments likely to restrict activity or mobility in older people (falls, memory difficulties, cough with spit, breathless when walking, dizziness, weakness in arms/legs, raised blood pressure). From these single items, counts of health conditions and impairments were calculated (0-12). Those indicating no conditions were compared to those who indicated any of the conditions.

6.4 Results of the mediation analyses

Tables 6.5 (ELSA) and 6.6 (NorStOP) display results of logistic regression testing the association between the predictor ("often troubled" with pain in ELSA and "any pain" in NorStOP) and each proposed mediator. The total, direct and indirect effects for each mediation model is also presented using all participants at baseline with complete data for all predictor, confounder and mediator information (ELSA n=6324, NorStOP n=10985).

6.4.1 Lifestyle factors

"Often troubled" with pain was associated with lower levels of physical activity and low alcohol consumption but was not associated with smoking in the ELSA dataset (Table 6.5). In the NorStOP dataset "any pain" was associated with not smoking, low alcohol consumption, obesity, low physical activity (frequency go out/walk for 10 minutes) and with sleep problems (Table 6.6).

In ELSA the relationship between "often troubled" with pain and mortality was mediated by physical inactivity and low alcohol consumption but not smoking (Table 6.5).
In NorStOP there was an indirect effect from "any pain" to mortality via all lifestyle factors with the exception of alcohol consumption and obesity (Table 6.6).

Table 6.5 Pathways between 'often troubled with pain' and mortality via lifestyle, health, social and psychological factors for the for the ELSA complete case sample (n=6324): Direct, indirect and total effects.

Mediator	Association between often troubled with pain and potential mediator Adjusted OR (95%CI)	Pathway	Adjusted HR (95%CI)
Model	**-**	**Total effect (no mediators)**	**1.30 (1.12, 1.50)**
LIFESTYLE FACTORS			
Physical activity		Direct	1.14 (0.98, 1.33)
none/mild	Reference	Indirect	**1.14 (1.10, 1.20)**
moderate/vigorous	**0.34 (0.30, 0.39)**	Total	1.30 (1.14, 1.51)
Smoking		Direct	1.29 (1.12, 1.50)
Non-smoker	Reference	Indirect	1.01 (0.99, 1.02)
Current smoker	1.07 (0.92, 1.25)	Total	1.30 (1.14, 1.51)
Alcohol consumption		Direct	1.28 (1.12, 1.49)
< weekly (low)	Reference	Indirect	**1.01 (1.00, 1.02)**
> weekly (high)	**0.71 (0.64, 0.80)**	Total	1.30 (1.14, 1.51)
HEALTH			
Self-reported health		Direct	0.99 (0.84, 1.16)
Poor/Fair	Reference	Indirect	**1.32 (1.23, 1.41)**
Good/Very good/Excellent	**0.18 (0.16, 0.21)**	Total	1.30 (1.14, 1.52)
Functional limitation (ADL/IADL difficulties)		Direct	1.00 (0.86, 1.16)
No difficulties	Reference	Indirect	**1.31 (1.20, 1.39)**
Any difficulties	**6.40 (5.61, 7.31)**	Total	1.31 (1.14, 1.51)
Symptoms preventing walking ¼ mile		Direct	0.89 (0.78, 1.04)
No symptoms	Reference	Indirect	**1.45 (1.35, 1.58)**
Any symptoms	**8.17 (7.08, 9.45)**	Total	1.30 (1.13, 1.51)
SOCIAL FACTORS			
Social group membership		Direct	1.29 (1.12, 1.50)
0-1 group	Reference	Indirect	**1.01 (1.00, 1.02)**
2 or more groups	**0.86 (0.77, 0.96)**	Total	1.30 (1.14, 1.51)
Volunteer work		Direct	1.29 (1.12, 1.50)
None	Reference	Indirect	**1.01 (1.00, 1.02)**
Any	**0.85 (0.76, 0.96)**	Total	1.30 (1.14, 1.51)

PSYCHOLOGICAL FACTORS			
Quality of life		Direct	1.18 (1.02, 1.36)
< median (low)	Reference	Indirect	**1.10 (1.07, 1.14)**
>median (high)	**0.37 (0.33, 0.41)**	Total	1.30 (1.13, 1.51)
Control		Direct	1.23 (1.07, 1.44)
< median (low)	Reference	Indirect	**1.06 (1.03, 1.08)**
>median (high)	**0.46 (0.41, 0.52)**	Total	1.30 (1.14, 1.51)
Autonomy		Direct	1.22 (1.06, 1.41)
< median(low)	Reference	Indirect	**1.07 (1.03, 1.10)**
>median(high)	**0.38 (0.34, 0.42)**	Total	1.30 (1.14, 1.51)
Pleasure		Direct	1.27 (1.11, 1.49)
< median (low)	Reference	Indirect	**1.02 (1.00, 1.04)**
>median (high)	**0.63 (0.56, 0.70)**	Total	1.30 (1.14, 1.51)
Self-realisation		Direct	1.24 (1.06, 1.41)
< median (low)	Reference	Indirect	**1.05 (1.03, 1.08**)
>median (high)	**0.48 (0.43, 0.54)**	Total	1.30 (1.14, 1.51)
Depression		Direct	1.20 (1.04, 1.38)
Not depressed (CESD score) <4	Reference	Indirect	**1.09 (1.05, 1.12)**
Depressed >4	**2.62 (2.33, 2.95)**	Total	1.30 (1.13, 1.51)
Cognitive impairment		Direct	1.29 (1.12, 1.49)
< median (low ability)	Reference	Indirect	**1.01 (1.00, 1.02)**
> median (high ability)	**0.83 (0.74, 0.93)**	Total	1.30 (1.13, 1.51)

All models adjusted for age, sex, education and wealth
OR = Odds ratio
HR = Hazard ratio
CI = Confidence Intervals
Significant associations between predictor and mediator and indirect effects are in **bold**

Table 6.6 Pathways between 'any pain' and mortality via lifestyle, health, social and psychological factors for the NorStOP complete case baseline sample (n=10985): Direct, indirect and total effects.

Mediator	Association between any pain and potential mediator Adjusted OR (95%CI)	Pathway	Adjusted HR (95%CI)
Model	-	**Total effect (no mediators)**	1.06 (0.95, 1.19)
LIFESTYLE FACTORS			
Smoking		Direct	1.05 (0.96, 1.17)
Never/Previous	Reference	Indirect	**1.01 (1.00, 1.02)**
Current	**0.88 (0.81, 0.97)**	Total	1.06 (0.96, 1.18)
Alcohol consumption		Direct	1.06 (0.96, 1.18)
Monthly or less (low)	Reference	Indirect	1.00 (1.00, 1.01)
Weekly (high)	**0.89 (0.81, 0.97)**	Total	1.06 (0.96, 1.18)
Obesity		Direct	1.06 (0.96, 1.18)
Not obese	Reference	Indirect	1.00 (0.99, 1.01)
Obese	**1.77 (1.57, 1.99)**	Total	1.06 (0.96, 1.18)
Frequency go out		Direct	0.96 (0.88, 1.07)
Few/No days (low)	Reference	Indirect	**1.09 (1.07, 1.12)**
All/Most/Some days (high)	**0.41 (0.35, 0.48)**	Total	1.05 (0.96, 1.17)
Frequency walk for 10 minutes		Direct	0.98 (0.88, 1.09)
< weekly (low)	Reference	Indirect	**1.09 (1.07, 1.10)**
>weekly (high)	**0.53 (0.49, 0.58)**	Total	1.06 (0.97, 1.19)
Sleep			
Trouble falling asleep		Direct	1.04 (0.94, 1.16)
Some/none	Reference	Indirect	**1.02 (1.00, 1.04)**
Most nights	**3.37 (2.84, 4.02)**	Total	1.05 (0.96, 1.17)
Wake in the night		Direct	1.01 (0.92, 1.12)
Some/none	Reference	Indirect	**1.03 (1.01, 1.06)**
Most nights	**2.56 (2.28, 2.88)**	Total	1.05 (0.95, 1.17)
Trouble staying asleep		Direct	1.04 (0.95, 1.15)
Some/none	Reference	Indirect	**1.02 (1.00, 1.04)**
Most nights	**2.87 (2.51, 3.28)**	Total	1.06 (0.96, 1.18)
Wake up unrefreshed		Direct	0.99 (0.90, 1.10)
Some/none	Reference	Indirect	**1.06 (1.03, 1.08)**
Most nights	**3.99 (3.40, 4.71)**	Total	1.04 (0.96, 1.16)

HEALTH FACTORS			
Self-rated health		Direct	0.84 (0.77, 0.93)
Fair/Poor	Reference	Indirect	**1.23 (1.20, 1.29)**
Excellent/Very good/Good	**0.28 (0.25, 0.31)**	Total	1.03 (0.94, 1.15)
Functional limitation (SF36)		Direct	0.84 (0.77, 0.93)
< median (low)	Reference	Indirect	**1.22 (1.16, 1.28)**
> median (high)	**0.15 (0.14, 0.17)**	Total	1.02 (0.93, 1.14)
SOCIAL FACTORS			
Social participation (restriction) (KAP)		Direct	0.97 (0.89, 1.09)
None	Reference	Indirect	**1.09 (1.07, 1.11)**
Any	**1.98 (1.81, 2.16)**	Total	1.05 (0.96, 1.18)
PSYCHOLOGICAL FACTORS			
Anxiety (HADS)		Direct	1.03 (0.93, 1.15)
No anxiety	Reference	Indirect	**1.04 (1.02, 1.06)**
Possible/probable	**2.58 (2.34, 2.85)**	Total	1.07 (0.97, 1.19)
Depression (HADS)		Direct	0.98 (0.89, 1.10)
No depression	Reference	Indirect	**1.08 (1.06, 1.11)**
Possible/probable	**2.88 (2.51, 3.31)**	Total	1.06 (0.96, 1.19)
Cognitive impairment		Direct	0.99 (0.90, 1.10)
No impairment	Reference	Indirect	**1.06 (1.04, 1.10)**
Impairment	**2.62 (2.39, 2.87)**	Total	1.05 (0.96, 1.17)
Control (from IPQ-R)		Direct	1.06 (0.97, 1.18)
Disagree (low control)	Reference	Indirect	1.00 (1.00, 1.00)
Agree (high control)	**0.91 (0.83, 1.00)**	Total	1.06 (0.97, 1.18)

All models adjusted for age, sex, education and wealth
OR = Odds ratio
HR = Hazard ratio
CI = Confidence Intervals
Significant associations between predictor and mediator and indirect effects are in **bold**

6.4.2 Health factors

In both ELSA and NorStOP all health factors were detrimentally associated with “often troubled” with pain and “any pain” respectively. There were statistically significant mediating/indirect effects of all health factors in both data samples (Table 6.5 and 6.6).

6.4.3 Social factors

All social factors were adversely associated with pain report in ELSA and NorStOP. There were statistically significant mediating effects of low social group membership and no volunteer work in ELSA and a statistically significant indirect effect via social participation restriction in NorStOP (Table 6.5 and 6.6).

6.4.4 Psychological factors

“Often troubled” with pain was associated with lower quality of life across all domains and with depression and cognitive impairment in the ELSA sample (Table 6.5). In NorStOP, “any pain” was associated with anxiety, depression, cognitive impairment and low perceived control of health (Table 6.6). There were statistically significant mediating/indirect effects of all psychological factors with the exception of perceived control of health in the NorStOP sample (Tables 6.5 and 6.6).

6.5 Results of the moderation analyses

6.5.1 Stratification by sex

Table 6.7 and 6.8 display the results of the logistic regression and mediation analyses stratified by sex in the ELSA and NorStOP samples respectively.

Table 6.7 Pathways between 'often troubled with pain' and mortality via lifestyle, health, social and psychological factors in the ELSA complete case sample (n=6324) stratified by sex: Direct, indirect and total effects.

	Females (n=3451)			Males (n=2873)		
	Association between often troubled with pain and potential mediator Adjusted OR (95%CI)	**Pathway**	**Adjusted HR (95%CI)**	**Association between often troubled with pain and potential mediator Adjusted OR (95%CI)**	**Pathway**	**Adjusted HR (95%CI)**
Model	**-**	**Total effect (no mediators)**	**1.24 (1.00, 1.53)**	**-**	**Total effect (no mediators)**	**1.36 (1.12, 1.66)**
LIFESTYLE FACTORS						
Physical activity		Direct	1.07 (0.87, 1.34)		Direct	1.21 (0.98, 1.41)
none/mild	Reference	Indirect	**1.16 (1.09, 1.22)**	Reference	Indirect	**1.13 (1.08, 1.19)**
moderate/vigorous	**0.33 (0.28, 0.40)**	Total	1.24 (1.00, 1.54)	**0.34 (0.28, 0.43)**	Total	1.36 (1.12, 1.62)
Smoking		Direct	1.23 (0.99, 1.55)		Direct	1.35 (1.10, 1.60)
Non-smoker	Reference	Indirect	1.00 (0.99, 1.02)	Reference	Indirect	1.01 (0.99, 1.02)
Current smoker	1.05 (0.85, 1.29)	Total	1.24 (1.00, 1.54)	1.10 (0.88, 1.37)	Total	1.36 (1.11, 1.61)
Alcohol consumption		Direct	1.21 (0.98, 1.51)		Direct	1.36 (1.11, 1.61)
< weekly (low)	Reference	Indirect	**1.02 (1.00, 1.04)**	Reference	Indirect	1.00 (0.99, 1.02)
> weekly (high)	**0.75 (0.65, 0.87)**	Total	1.24 (1.00, 1.54)	**0.65 (0.55, 0.78)**	Total	1.36 (1.11, 1.61)
HEALTH						
Self-reported health		Direct	0.97 (0.78, 1.25)		Direct	1.00 (0.81, 1.24)
Poor/Fair	Reference	Indirect	**1.27 (1.16, 1.38)**	Reference	Indirect	**1.36 (1.26, 1.45)**
Good/Very good/Excellent	**0.18 (0.15, 0.22)**	Total	1.24 (1.00, 1.53)	**0.18 (0.15, 0.22)**	Total	1.36 (1.12, 1.63)
Functional limitation (ADL/IADL difficulties)		Direct	0.95 (0.75, 1.25)		Direct	1.04 (0.84, 1.23)
No difficulties	Reference	Indirect	**1.30 (1.19, 1.41)**	Reference	Indirect	**1.32 (1.21, 1.45)**
Any difficulties	**6.02 (5.07, 7.17)**	Total	1.24 (1.00, 1.53)	**6.97 (5.68, 8.56)**	Total	1.37 (1.13, 1.61)

Symptoms preventing walking ¼ mile		Direct	0.87 (0.69, 1.15)		Direct	0.91 (0.74, 1.11)
No symptoms	Reference	Indirect	**1.43 (1.26, 1.57)**	Reference	Indirect	**1.48 (1.36, 1.64)**
Any symptoms	**7.33 (6.06, 8.89)**	Total	1.24 (0.98, 1.55)	**9.44 (7.60, 11.78)**	Total	1.35 (1.11, 1.59)
SOCIAL FACTORS						
Social group membership		Direct	1.23 (0.99, 1.53)		Direct	1.34 (1.09, 1.60)
0-1 group	Reference	Indirect	1.00 (1.00, 1.01)	Reference	Indirect	**1.01 (1.00, 1.03)**
2 or more groups	0.91 (0.79, 1.06)	Total	1.24 (1.00,1.54)	**0.79 (0.67, 0.94)**	Total	1.36 (1.11, 1.61)
Volunteer work		Direct	1.23 (1.00, 1.53)		Direct	1.35 (1.10, 1.59)
None	Reference	Indirect	**1.01 (1.00, 1.02)**	Reference	Indirect	**1.01 (1.00, 1.02)**
Any	0.87 (0.74, 1.01)	Total	1.24 (1.00, 1.54)	**0.83 (0.69, 1.00)**	Total	1.36 (1.11, 1.61)
PSYCHOLOGICAL FACTORS						
Quality of life		Direct	1.11 (0.89, 1.40)		Direct	1.24 (0.99, 1.49)
< median (low)	Reference	Indirect	**1.11 (1.05, 1.16)**	Reference	Indirect	**1.09 (1.04, 1.14)**
>median (high)	**0.37 (0.32, 0.42)**	Total	1.24 (1.00, 1.54)	**0.36 (0.31, 0.43)**	Total	1.36 (1.11, 1.61)
Control		Direct	1.16 (0.95, 1.44)		Direct	1.30 (1.06, 1.56)
< median (low)	Reference	Indirect	**1.07 (1.03, 1.10)**	Reference	Indirect	**1.04 (1.02, 1.07)**
>median (high)	**0.46 (0.39, 0.53)**	Total	1.24 (1.00, 1.55)	**0.46 (0.39, 0.55)**	Total	1.36 (1.11, 1.61)
Autonomy		Direct	1.16 (0.93, 1.42)		Direct	1.28 (1.03, 1.53)
< median(low)	Reference	Indirect	**1.07 (1.01, 1.12)**	Reference	Indirect	**1.07 (1.02, 1.11)**
>median(high)	**0.37 (0.31, 0.42)**	Total	1.23 (0.99, 1.55)	**0.40 (0.33, 0.47)**	Total	1.37 (1.11, 1.61)
Pleasure		Direct	1.19 (0.95, 1.44)		Direct	1.35 (1.10, 1.62)
< median (low)	Reference	Indirect	**1.04 (1.01, 1.07)**	Reference	Indirect	1.01 (0.99, 1.03)
>median (high)	**0.62 (0.54, 0.71)**	Total	1.24 (1.00, 1.55)	**0.64 (0.54, 0.75)**	Total	1.36 (1.11, 1.61)
Self-realisation		Direct	1.17 (0.95, 1.46)		Direct	1.30 (1.05, 1.55)
< median (low)	Reference	Indirect	**1.06 (1.03, 1.09)**	Reference	Indirect	**1.05 (1.02, 1.08)**
>median (high)	**0.49 (0.42, 0.56)**	Total	1.24 (1.00, 1.54)	**0.47 (0.40, 0.57)**	Total	1.37 (1.12, 1.62)
Depression		Direct	1.21 (1.00, 1.51)		Direct	1.18 (0.98, 1.42)
Not depressed (CESD score) <4	Reference	Indirect	1.02 (0.99, 1.07)	Reference	Indirect	**1.15 (1.10, 1.22)**
Depressed >4	**2.42 (2.08, 2.82)**	Total	1.24 (1.00, 1.54)	**2.97 (2.45, 3.59)**	Total	1.36 (1.12, 1.62)

Cognitive impairment		Direct	1.23 (0.99, 1.53)		Direct	1.35 (1.09, 1.60)
< median (low ability)	Reference	Indirect	**1.01 (1.00, 1.02)**	Reference	Indirect	**1.01 (1.00, 1.02)**
> median (high ability)	0.89 (0.76, 1.03)	Total	1.24 (1.00, 1.54)	**0.76 (0.64, 0.90)**	Total	1.36 (1.11, 1.61)

All models adjusted for age, sex, education and wealth
OR = Odds ratio
HR = Hazard ratio
CI = Confidence Intervals
Significant associations between predictor and mediator and indirect effects are in **bold**

Table 6.8 Pathways between 'any pain' and mortality via lifestyle, health, social and psychological factors for the NorStOP complete case baseline sample (n=10985): Direct, indirect and total effects stratified by sex.						
	Females (n=5967)			**Males (n=5018)**		
	Association between any pain and potential mediator Adjusted OR (95%CI)	**Pathway**	**Adjusted HR (95%CI)**	**Association between any pain and potential mediator Adjusted OR (95%CI)**	**Pathway**	**Adjusted HR (95%CI)**
Model	**-**	**Total effect (no mediators)**	1.03 (0.87, 1.21)	**-**	**Total effect (no mediators)**	1.08 (0.92, 1.26)
LIFESTYLE FACTORS						
Smoking		Direct	1.02 (0.87, 1.17)		Direct	1.06 (0.94, 1.28)
Never/Previous	Reference	Indirect	1.00 (0.99, 1.01)	Reference	Indirect	**1.02 (1.01, 1.03)**
Current	0.98 (0.88,1.10)	Total	1.03 (0.88, 1.17)	**0.75 (0.66, 0.87)**	Total	1.08 (0.96, 1.30)
Alcohol consumption		Direct	1.02 (0.88, 1.17)		Direct	1.08 (0.96, 1.30)
Monthly or less (low)	Reference	Indirect	1.00 (1.00, 1.01)	Reference	Indirect	1.00 (1.00, 1.00)
Weekly (high)	**0.86 (0.77, 0.97)**	Total	1.03 (0.88, 1.18)	0.92 (0.80, 1.06)	Total	1.08 (0.96, 1.30)
Obesity		Direct	1.02 (0.87, 1.17)		Direct	1.08 (0.96, 1.30)
Not obese	Reference	Indirect	1.01 (0.98, 1.02)	Reference	Indirect	1.00 (0.99, 1.01)
Obese	**2.04 (1.73, 2.41)**	Total	1.03 (0.88, 1.18)	**1.50 (1.26, 1.78)**	Total	1.08 (0.96, 1.30)
Frequency go out		Direct	0.89 (0.76, 1.01)		Direct	1.02 (0.90, 1.22)
Few/No days (low)	Reference	Indirect	**1.14 (1.10, 1.18)**	Reference	Indirect	**1.03 (1.04, 1.08)**
All/Most/Some days (high)	**0.38 (0.31, 0.46)**	Total	1.02 (0.87, 1.17)	**0.47 (0.37, 0.59)**	Total	1.07 (0.96, 1.29)
Frequency walk for 10 minutes		Direct	0.92 (0.79, 1.05)		Direct	1.02 (0.90, 1.21)
< weekly (low)	Reference	Indirect	**1.12 (1.08, 1.15)**	Reference	Indirect	**1.06 (1.04, 1.08)**
>weekly (high)	**0.49 (0.42, 0.54)**	Total	1.03 (0.88, 1.19)	**0.60 (0.53, 0.68)**	Total	1.08 (0.96, 1.29)

Sleep						
Trouble falling asleep		Direct	0.98 (0.85, 1.13)		Direct	1.08 (0.96, 1.32)
Some/none	Reference	Indirect	**1.03 (1.01, 1.06)**	Reference	Indirect	1.00 (0.98, 1.03)
Most nights	**3.27 (2.66, 4.06)**	Total	1.01 (0.87, 1.15)	**3.56 (2.65, 4.88)**	Total	1.08 (0.96, 1.31)
Wake in the night		Direct	0.97 (0.84, 1.13)		Direct	1.04 (0.91, 1.27)
Some/none	Reference	Indirect	**1.03 (1.01, 1.06)**	Reference	Indirect	**1.04 (1.01, 1.06)**
Most nights	**2.62 (2.24, 3.07)**	Total	1.00 (0.86, 1.15)	**2.48 (2.08, 2.99)**	Total	1.08 (0.95, 1.31)
Trouble staying asleep		Direct	0.99 (0.85, 1.14)		Direct	1.08 (0.96,1.30)
Some/none	Reference	Indirect	**1.03 (1.00, 1.05)**	Reference	Indirect	1.01 (0.99, 1.03)
Most nights	**2.76 (2.34, 3.28)**	Total	1.01 (0.87, 1.16)	**3.03 (2.45, 3.79)**	Total	1.09(0.97, 1.32)
Wake up unrefreshed		Direct	0.95 (0.82, 1.10)		Direct	1.01 (0.90, 1.22)
Some/none	Reference	Indirect	**1.05 (1.02, 1.10)**	Reference	Indirect	**1.06 (1.03, 1.08)**
Most nights	**4.07 (3.32, 5.04)**	Total	1.00 (0.87, 1.15)	**3.86 (3.00, 5.05)**	Total	1.07 (0.95, 1.29)
HEALTH FACTORS						
Self-rated health		Direct	0.81 (0.70, 0.95)		Direct	0.87 (0.77, 1.05)
Fair/Poor	Reference	Indirect	**1.24 (1.18, 1.30)**	Reference	Indirect	**1.22 (1.17, 1.28)**
Excellent/Very good/Good	**0.25 (0.21, 0.29)**	Total	1.01 (0.86, 1.16)	**0.32 (0.27, 0.37)**	Total	1.05 (0.95, 1.26)
Functional ability (SF36)		Direct	0.84 (0.70, 0.96)		Direct	0.84 (0.73, 0.99)
< median (low)	Reference	Indirect	**1.17 (1.10, 1.25)**	Reference	Indirect	**1.25 (1.18, 1.33)**
> median (high)	**0.14 (0.12, 0.16)**	Total	0.99 (0.85, 1.12)	**0.18 (0.15, 0.21)**	Total	1.05 (0.93, 1.24)
SOCIAL FACTORS						
Social participation (restriction) (KAP)		Direct	0.92 (0.79, 1.04)		Direct	1.01 (0.89, 1.23)
None	Reference	Indirect	**1.10 (1.08, 1.15)**	Reference	Indirect	**1.06 (1.04, 1.09)**
Any	**2.17 (1.92, 2.45)**	Total	1.02 (0.87, 1.16)	**1.78 (1.56, 2.02**)	Total	1.08 (0.96, 1.30)
PSYCHOLOGICAL FACTORS						
Anxiety (HADS)		Direct	0.99 (0.86, 1.16)		Direct	1.05 (0.93, 1.29)
No anxiety	Reference	Indirect	**1.04 (1.01, 1.07)**	Reference	Indirect	**1.04 (1.00, 1.06)**
Possible/probable	**2.45 (2.16, 2.78)**	Total	1.03 (0.86, 1.19)	**2.80 (2.39, 3.29)**	Total	1.09 (0.97, 1.34)

Depression (HADS)		Direct	0.92 (0.79, 1.06)		Direct	1.02 (0.90, 1.24)
No depression	Reference	Indirect	**1.11 (1.08, 1.16)**	Reference	Indirect	**1.06 (1.03, 1.08)**
Possible/probable	**3.13 (2.60, 3.81)**	Total	1.01 (0.87, 1.17)	**2.62 (2.16, 3.20)**	Total	1.08 (0.96, 1.31)
Cognitive impairment		Direct	0.92 (0.78, 1.08)		Direct	1.04 (0.92, 1.24)
No impairment	Reference	Indirect	**1.10 (1.06, 1.13)**	Reference	Indirect	**1.04 (1.00, 1.06)**
Impairment	**2.66 (2.35, 3.02)**	Total	1.01 (0.88, 1.16)	**2.56 (2.23, 2.95)**	Total	1.08 (0.96, 1.30)
Control (from IPQ-R)		Direct	1.03 (0.88, 1.18)		Direct	1.08 (0.96, 1.30)
Disagree (low control)	Reference	Indirect	1.00 (0.99, 1.00)	Reference	Indirect	1.00 (1.00, 1.00)
Agree (high control)	**0.87 (0.77, 0.99)**	Total	1.03 (0.88, 1.18)	0.96 (0.84, 1.10)	Total	1.08 (0.96, 1.30)

All models adjusted for age, sex, education and adequacy of income
OR = Odds ratio
HR = Hazard ratio
CI = Confidence Intervals
Significant associations between predictor and mediator and indirect effects are in **bold**

"Often troubled" with pain was associated with all proposed mediating factors in females in the ELSA sample with the exception of smoking, social group membership, volunteer work and cognitive impairment. In males, only smoking was not associated with "often troubled" with pain (Table 6.7). In the NorStOP sample, in females all proposed mediators with the exception of smoking were associated with "any pain". In males, alcohol consumption and perceived control over health were the only proposed mediators not statistically significantly associated with "any pain" (Table 6.8).

Sex did not moderate the relationship between "often troubled" with pain in ELSA or between "any pain" and mortality in NorStOP.

In ELSA, sex moderated the relationship between "often troubled" with pain and mortality via depression. There was a significant mediating effect in males but not in females and this difference was statistically significant as the confidence intervals did not overlap between strata (Table 6.7). Conversely, in the NorStOP sample, there was a statistically significant indirect effect of depression in females and males but the effect size was larger in females. Again the confidence intervals did not overlap between strata indicating a statistically significant difference between the groups (Table 6.8).

In the NorStOP sample sex moderated the indirect effects between "any pain" and mortality via (not) smoking (stronger in males), low frequency of going out, low frequency of walking for 10 minutes and cognitive impairment (stronger in females) (Table 6.8).

6.5.2 Stratification by comorbidity

Tables 6.9 and 6.10 display the results of logistic regression and of the mediation analyses of the ELSA and NorStOP samples described in section 6.5 stratified by comorbidity.

In ELSA, “often troubled” with pain was adversely associated with social group membership and volunteer work in participants with comorbidity but not in those without. All other proposed mediators were associated with “often troubled” with pain in both strata with the exception of smoking which was not significantly associated with “often troubled” with pain in either stratum (Table 6.9).

In NorStOP, smoking was not associated with “any pain” in participants with comorbidity and alcohol consumption and perceived control over health were not associated with “any pain” in participants without comorbidity. All other proposed mediators were associated with “any pain” in both strata (Table 6.10).

Comorbidity did not moderate the relationship between “often troubled” with pain and mortality in ELSA or the relationship between “any pain” and mortality in NorStOP (Tables 6.9 and 6.10).

Comorbidity did not significantly moderate any of the mediated pathways in the ELSA samples as the confidence intervals for the indirect effects of all variables overlapped between sub-groups with the exception of the ‘pleasure’ domain of quality of life. Low ‘pleasure’ mediated the relationship between “often troubled” with pain and mortality in participants without comorbidity only (Table 6.9).

In NorStOP, comorbidity moderated the indirect effects between “any pain” and mortality via low frequency of going out, low frequency of walking for 10 minutes,

Table 6.9 Pathways between 'often troubled with pain' and mortality via lifestyle, health, social and psychological factors in the ELSA complete case sample (n=6324) stratified by comorbidity: Direct, indirect and total effects.						
	With comorbidity (n=3739)			**No comorbidity (n=2585)**		
	Association between often troubled with pain and potential mediator Adjusted OR (95%CI)	**Pathway**	**Adjusted HR (95%CI)**	**Association between often troubled with pain and potential mediator OR (95%CI)**	**Pathway**	**Adjusted HR (95%CI)**
Model	-	**Total effect (no mediators)**	**1.26 (1.06, 1.49)**	-	**Total effect (no mediators)**	1.19 (0.85, 1.67)
LIFESTYLE FACTORS						
Physical activity		Direct	1.11 (0.95, 1.32)		Direct	1.08 (0.72, 1.50)
none/mild	Reference	Indirect	**1.13 (1.09, 1.18)**	Reference	Indirect	**1.14 (1.07, 1.20)**
moderate/vigorous	**0.35 (0.30, 0.42)**	Total	1.26 (1.05, 1.48)	**0.39 (0.30, 0.51)**	Total	1.23 (0.79, 1.69)
Smoking		Direct	1.24 (1.04, 1.46)		Direct	1.20 (0.78, 1.70)
Non-smoker	Reference	Indirect	**1.01 (1.00, 1.03)**	Reference	Indirect	1.00 (0.98, 1.01)
Current smoker	1.18 (0.97, 1.44)	Total	1.26 (1.05, 1.48)	0.95 (0.72, 1.25)	Total	1.19 (0.76, 1.68)
Alcohol consumption		Direct	1.24 (1.03, 1.45)		Direct	1.20 (0.75, 1.73)
< weekly (low)	Reference	Indirect	**1.02 (1.00, 1.03)**	Reference	Indirect	1.00 (0.97, 1.02)
> weekly (high)	**0.75 (0.65, 0.86)**	Total	1.26 (1.05, 1.48)	**0.69 (0.56, 0.85)**	Total	1.19 (0.76, 1.69)
HEALTH						
Self-reported health		Direct	0.96 (0.81, 1.13)		Direct	1.00 (0.65, 1.39)
Poor/Fair	Reference	Indirect	**1.29 (1.21, 1.40)**	Reference	Indirect	**1.17 (1.08, 1.31)**
Good/Very good/Excellent	**0.23 (0.19, 0.25)**	Total	1.25 (1.05, 1.47)	**0.25 (0.19, 0.33)**	Total	1.17 (0.73, 1.69)

Functional limitation						
(ADL/IADL difficulties)		Direct	1.00 (0.82, 1.17)		Direct	0.95 (0.59, 1.34)
No difficulties	Reference	Indirect	**1.25 (1.16, 1.34)**	Reference	Indirect	**1.27 (1.16, 1.43)**
Any difficulties	**5.76 (4.92, 6.76)**	Total	1.25 (1.05, 1.46)	**4.67 (3.57, 6.11)**	Total	1.20 (0.76, 1.75)
Symptoms preventing walking ¼ mile		Direct	0.86 (0.72, 1.06)		Direct	0.95 (0.58, 1.36)
No symptoms	Reference	Indirect	**1.45 (1.34, 1.55)**	Reference	Indirect	**1.21 (1.08, 1.36)**
Any symptoms	**6.83 (5.78, 8.10)**	Total	1.25 (1.04, 1.47)	**6.39 (4.70, 8.73)**	Total	1.15 (0.76, 1.64)
SOCIAL FACTORS						
Social group membership		Direct	1.24 (1.04, 1.46)		Direct	1.19 (0.76, 1.66)
0-1 group	Reference	Indirect	**1.01 (1.00, 1.02)**	Reference	Indirect	1.00 (0.99, 1.02)
2 or more groups	**0.80 (0.69, 0.92)**	Total	1.26 (1.05, 1.48)	0.94 (0.77, 1.15)	Total	1.19 (0.76, 1.68)
Volunteer work		Direct	1.24 (1.04, 1.45)		Direct	1.19 (0.76, 1.66)
None	Reference	Indirect	**1.01 (1.00, 1.02)**	Reference	Indirect	1.00 (0.99, 1.02)
Any	**0.80 (0.69, 0.93)**	Total	1.26 (1.05, 1.48)	0.98 (0.79, 1.21)	Total	1.19 (0.76, 1.67)
PSYCHOLOGICAL FACTORS						
Quality of life		Direct	1.15 (0.97, 1.39)		Direct	1.10 (0.69, 1.52)
< median (low)	Reference	Indirect	**1.09 (1.05, 1.13)**	Reference	Indirect	**1.09 (1.04, 1.15)**
>median (high)	**0.37 (0.32, 0.43)**	Total	1.25 (1.05, 1.47)	**0.50 (0.41, 0.62)**	Total	1.20 (0.75, 1.70)
Control		Direct	1.19 (1.00, 1.41)		Direct	1.15 (0.72, 1.62)
< median (low)	Reference	Indirect	**1.05 (1.03, 1.08)**	Reference	Indirect	**1.03 (1.00, 1.07)**
>median (high)	**0.48 (0.41, 0.56)**	Total	1.26 (1.05, 1.47)	**0.56 (0.46, 0.68)**	Total	1.18 (0.74, 1.68)
Autonomy		Direct	1.19 (1.01, 1.42)		Direct	1.12 (0.71, 1.56)
< median(low)	Reference	Indirect	**1.05 (1.02, 1.09)**	Reference	Indirect	**1.06 (1.02, 1.11)**
>median(high)	**0.37 (0.32, 0.43)**	Total	1.26 (1.06, 1.48)	**0.53 (0.44, 0.65)**	Total	1.20 (0.76, 1.69)
Pleasure		Direct	1.25 (1.05, 1.47)		Direct	1.14 (0.73, 1.61)
< median (low)	Reference	Indirect	1.01 (0.99, 1.02)	Reference	Indirect	**1.06 (1.02, 1.10)**
>median (high)	**0.66 (0.57, 0.75)**	Total	1.26 (1.05, 1.48)	**0.64 (0.53, 0.78)**	Total	1.20 (0.76, 1.72)
Self-realisation		Direct	1.20 (1.00, 1.43)		Direct	1.16 (0.73, 1.60)
< median (low)	Reference	Indirect	**1.04 (1.02, 1.07)**	Reference	Indirect	**1.05 (1.02, 1.08)**
>median (high)	**0.49 (0.42, 0.56)**	Total	1.26 (1.05, 1.48)	**0.61 (0.50, 0.75)**	Total	1.21 (0.77, 1.70)

Depression		Direct	1.16 (0.96, 1.36)		Direct	1.14 (0.74, 1.57)
Not depressed (CESD score) <4	Reference	Indirect	**1.08 (1.03, 1.12)**	Reference	Indirect	**1.05 (1.01, 1.10)**
Depressed >4	**2.58 (2.23, 2.99**)	Total	1.25 (1.05, 1.46)	**1.90 (1.51, 2.38)**	Total	1.20 (0.77, 1.68)
Cognitive impairment		Direct	1.25 (1.05, 1.47)		Direct	1.18 (0.76, 1.68)
< median (low ability)	Reference	Indirect	**1.01 (1.00, 1.02)**	Reference	Indirect	**1.02 (1.00, 1.04)**
> median (high ability)	**0.84 (0.73, 0.97)**	Total	1.26 (1.05, 1.48)	**0.80 (0.65, 0.98)**	Total	1.20 (0.76, 1.70)

All models adjusted for age, sex, education and wealth
OR = Odds ratio
HR = Hazard ratio
CI = Confidence Intervals
Significant associations between predictor and mediator and indirect effects are in **bold**

Table 6.10 Pathways between 'any pain' and mortality via lifestyle, health, social and psychological factors for the NorStOP complete case baseline sample (n=10985): Direct, indirect and total effects stratified by comorbidity.

	Comorbidity (n=9001)			No comorbidity (n=1984)		
	Association between any pain and potential mediator Adjusted OR (95%CI)	**Pathway**	**Adjusted HR (95%CI)**	**Association between any pain and potential mediator Adjusted OR (95%CI)**	**Pathway**	**Adjusted HR (95%CI)**
Model	-	**Total effect (no mediators)**	0.97 (0.86, 1.09)	-	**Total effect (no mediators)**	1.44 (0.98, 2.12)
LIFESTYLE FACTORS						
Smoking		Direct	0.96 (0.86, 1.09)		Direct	1.42 (0.99, 2.07)
Never/Previous	Reference	Indirect	1.00 (1.00, 1.01)	Reference	Indirect	**1.02 (1.00, 1.05)**
Current	0.97 (0.87, 1.07)	Total	0.97 (0.86, 1.09)	0.85 (0.71, 1.02)	Total	1.44 (1.00, 2.12)
Alcohol consumption		Direct	0.97 (0.86, 1.09)		Direct	1.45 (1.01, 2.13)
Monthly or less (low)	Reference	Indirect	1.00 (1.00, 1.01)	Reference	Indirect	0.99 (0.98, 1.01)
Weekly (high)	**0.85 (0.76, 0.94)**	Total	0.97 (0.86, 1.09)	1.14 (0.94, 1.37)	Total	1.44 (1.00, 2.10)
Obesity		Direct	0.97 (0.86, 1.09)		Direct	1.43 (0.99, 2.09)
Not obese	Reference	Indirect	1.00 (0.99, 1.01)	Reference	Indirect	1.00 (0.98, 1.03)
Obese	**1.60 (1.40, 1.83)**	Total	0.97 (0.87, 1.09)	**1.44 (1.08, 1.92)**	Total	1.44 (1.00, 2.09)
Frequency go out		Direct	0.88 (0.78, 0.99)		Direct	1.44 (1.01, 2.11)
Few/No days (low)	Reference	Indirect	**1.09 (1.07, 1.12)**	Reference	Indirect	1.01 (0.98, 1.04)
All/Most/Some days (high)	**0.44 (0.37, 0.52)**	Total	0.96 (0.86, 1.08)	**0.62 (0.40, 0.95)**	Total	1.45 (1.00, 2.12)
Frequency walk for 10 minutes		Direct	0.89 (0.79, 1.01)		Direct	1.45 (1.01, 2.10)
< weekly (low)	Reference	Indirect	**1.09 (1.07, 1.11)**	Reference	Indirect	1.00 (0.97, 1.03)
>weekly (high)	**0.54 (0.49, 0.60)**	Total	0.97 (0.86, 1.09)	**0.71 (0.59, 0.86)**	Total	1.44 (1.00, 2.13)

Sleep						
Trouble falling asleep		Direct	0.95 (0.86, 1.07)		Direct	1.42 (0.99, 2.08)
Some/none	Reference	Indirect	1.01 (0.99, 1.03)	Reference	Indirect	1.02 (0.98, 1.07)
Most nights	**3.01 (2.50, 3.65)**	Total	0.96 (0.87, 1.08)	**2.62 (1.64, 4.30)**	Total	1.44 (1.00, 2.13)
Wake in the night		Direct	0.94 (0.84, 1.05)		Direct	1.41 (0.97, 2.08)
Some/none	Reference	Indirect	**1.02 (1.01, 1.04)**	Reference	Indirect	1.03 (0.96, 1.10)
Most nights	**2.19 (1.93, 2.50)**	Total	0.96 (0.86, 1.08)	**2.85 (2.08, 3.95)**	Total	1.44 (1.01, 2.12)
Trouble staying asleep		Direct	0.95 (0.86, 1.07)		Direct	1.47 (1.01, 2.14)
Some/none	Reference	Indirect	1.01 (0.99, 1.03)	Reference	Indirect	0.97 (0.95, 1.02)
Most nights	**2.56 (2.21, 2.97)**	Total	0.96 (0.87, 1.08)	**2.37 (1.68, 3.38)**	Total	1.45 (1.00, 2.12)
Wake up unrefreshed		Direct	0.91 (0.81, 1.02)		Direct	1.49 (1.04, 2.18)
Some/none	Reference	Indirect	**1.05 (1.03, 1.07)**	Reference	Indirect	**0.97 (0.94, 1.00)**
Most nights	**3.32 (2.80, 3.97)**	Total	0.95 (0.86, 1.07)	**4.08 (2.55, 6.84)**	Total	1.45 (1.00, 2.12)
HEALTH FACTORS						
Self-rated health		Direct	0.79 (0.70, 0.89)		Direct	1.43 (1.02, 2.00)
Fair/Poor	Reference	Indirect	**1.20 (1.16, 1.23)**	Reference	Indirect	1.01 (0.97, 1.06)
Excellent/Very good/Good	**0.34 (0.30, 0.38)**	Total	0.95 (0.85, 1.07)	**0.24 (0.15, 0.37)**	Total	1.44 (1.02, 1.99)
Functional limitation (SF36)		Direct	0.80 (0.71, 0.90)		Direct	1.28 (0.79, 1.73)
< median (low)	Reference	Indirect	**1.18 (1.14, 1.23)**	Reference	Indirect	1.11 (0.94, 1.30)
> median (high)	**0.18 (0.16, 0.20)**	Total	0.94 (0.84, 1.05)	**0.15 (0.11, 0.21)**	Total	1.43 (1.00, 1.93)
SOCIAL FACTORS						
Social participation (restriction) (KAP)		Direct	0.89 (0.79, 1.00)		Direct	1.41 (0.99, 1.95)
None	Reference	Indirect	**1.08 (1.06, 1.11)**	Reference	Indirect	**1.02 (1.00, 1.05)**
Any	**1.98 (1.78, 2.19)**	Total	0.96 (0.86, 1.08)	**1.30 (1.07, 1.58)**	Total	1.44 (1.02, 1.96)
PSYCHOLOGICAL FACTORS						
Anxiety (HADS)		Direct	0.94 (0.84, 1.05)		Direct	1.50 (1.06, 2.06)
No anxiety	Reference	Indirect	**1.04 (1.02, 1.05)**	Reference	Indirect	0.96 (0.92, 1.00)
Possible/probable	**2.32 (2.08, 2.60)**	Total	0.98 (0.88, 1.09)	**2.07 (1.65, 2.61)**	Total	1.44 (1.02, 1.95)

Depression (HADS)		Direct	0.90 (0.81, 1.01)		Direct	1.42 (1.00, 1.94)
No depression	Reference	Indirect	**1.07 (1.06, 1.09)**	Reference	Indirect	1.02 (0.98, 1.06)
Possible/probable	**2.46 (2.13, 2.85)**	Total	0.97 (0.87, 1.09)	**2.48 (1.61, 3.93)**	Total	1.44 (1.02, 1.96)
Cognitive impairment		Direct	0.92 (0.82, 1.03)		Direct	1.37 (0.97, 1.87)
No impairment	Reference	Indirect	**1.04 (1.02, 1.07)**	Reference	Indirect	**1.05 (1.01, 1.12)**
Impairment	**2.26 (2.04, 2.51)**	Total	0.96 (0.86, 1.08)	**1.70 (1.30, 2.22)**	Total	1.43 (1.01, 1.94)
Control (from IPQ-R)		Direct	0.97 (0.86, 1.07)		Direct	1.44 (1.02, 1.97)
Disagree (low control) (Reference)	Reference	Indirect	1.00 (1.00, 1.00)	Reference	Indirect	1.00 (0.99, 1.02)
Agree (high control)	0.93 (0.83, 1.04)	Total	0.97 (0.86, 1.09)	0.89 (0.73, 1.08)	Total	1.44 (1.02, 1.97)

All models adjusted for age, sex, education and adequacy of income
OR = Odds ratio
HR = Hazard ratio
CI = Confidence Intervals
Significant associations between predictor and mediator and indirect effects are in **bold**

waking up unrefreshed, poor self-rated health, social participation restriction, anxiety and depression. For all of these mediators the indirect effects were greater in participants with comorbidity.

6.6 Allostatic load and Frailty (ELSA only)

6.6.1 Mediation by allostatic load

"Often troubled" with pain was significantly associated with high allostatic load (Table 6.11). There was a significant association between "often troubled" with pain and mortality in the allostatic load sample (n=4627). Allostatic load was a statistically significant mediator of the relationship between "often troubled" with pain and mortality in the total sample, and in males and females, but not in participants with or without comorbidity. There were no moderating effects of sex and comorbidity (Table 6.11).

6.6.2 Mediation by frailty

Frailty was strongly associated with "often troubled" with pain in the frailty sample (n=4375) (Table 6.12). Although there was not a significant association between "often troubled" with pain and mortality in this sample, there were significant indirect effects via frailty in females, males and in participants with and without comorbidity. There were no significant moderating effects of sex or comorbidity in this sample (Table 6.12).

Table 6.11 Pathways between 'often troubled with pain' and mortality via allostatic load in ELSA: Direct, indirect and total effects.					
Model	**Complete sample (n=4627)**	**Females (n=2539)**	**Males (n=2088)**	**With comorbidity (n=2704)**	**Without comorbidity (n=1923)**
Association between 'often troubled' with pain and allostatic load **Adjusted OR (95%CI)** *<median (low)* *> median(high)*	Reference **1.20 (1.06, 1.37)**	Reference **1.20 (1.01,1.41)**	Reference **1.22 (1.00, 1.48)**	Reference **1.13 (0.96, 1.32)**	Reference **1.16 (0.92, 1.46)**
Total effect (no mediator) **Adjusted HR (95%CI)**	1.21 (1.03, 1.44)	1.08 (0.84, 1.38)	1.35 (1.07, 1.69)	1.18 (0.97, 1.44)	1.13 (0.78, 1.63)
Pathway Adjusted HR(95%CI)					
Direct	1.20 (1.02, 1.41)	1.07 (0.85, 1.42)	1.33 (1.07, 1.71)	1.17 (0.96, 1.45)	1.14 (0.78, 1.53)
Indirect	**1.01 (1.00, 1.02)**	**1.01 (1.00, 1.03)**	**1.01 (1.00, 1.02)**	1.01(0.99, 1.03)	0.99 (0.76, 1.53)
Total	1.21 (1.03, 1.42)	1.08 (0.85, 1.44)	1.34 (1.07, 1.71)	1.18 (0.98, 1.48)	1.13 (0.77, 1.53)
All models adjusted for age, sex, education and wealth OR = Odds ratio HR = Hazard ratio CI = Confidence Intervals Significant associations between predictor and mediator and indirect effects are in **bold**					

Table 6.12 Pathways between 'often troubled with pain' and mortality via frailty in ELSA: Direct, indirect and total effects.

Model	Complete sample (n=4375)	Females (n=2400)	Males (n=1975)	With comorbidity (n=2835)	Without comorbidity (n=1540)
Association between 'often troubled and frailty Adjusted OR (95%CI)					
Not frail	Reference	Reference	Reference	Reference	Reference
vs frail	**3.33 (2.61, 4.27)**	**3.58 (2.64, 4.91)**	**2.97 (1.99, 4.46)**	**3.22 (2.42, 4.34)**	**2.95 (1.72, 5.00)**
Total effect (no mediator) Adjusted HR (95%CI)	1.10 (0.96, 1.27)	1.07 (0.87, 1.31)	1.15 (0.94, 1.41)	1.01 (0.86, 1.20)	1.31 (0.95, 1.81)
Pathway Adjusted HR(95%CI)					
Direct	1.02 (0.88, 1.21)	0.97 (0.82, 1.16)	1.09 (0.89, 1.34)	0.94 (0.77, 1.13)	1.24 (0.88, 1.65)
Indirect	**1.08 (1.05, 1.12)**	**1.11 (1.05, 1.17)**	**1.06 (1.02, 1.11)**	**1.08 (1.05, 1.12)**	**1.07 (1.02, 1.14)**
Total	1.11 (0.95, 1.29)	1.07 (0.90, 1.27)	1.15 (0.92, 1.42)	1.01 (0.84, 1.22)	1.34 (0.93, 1.76)

All models adjusted for age, sex, education and wealth
OR = Odds ratio
HR = Hazard ratio
CI = Confidence Intervals
Significant associations between predictor and mediator and indirect effects are in **bold**

6.7 Discussion

6.7.1 Summary of findings

Table 6.13 summarises which factors were mediators in each of the samples from each dataset.

6.7.2 Interpretation of findings

In general, a larger indirect effect indicates a more powerful explanation of the relationship under investigation (Keele, 2015). Based on this, the most powerful explanatory factors for a relationship between pain and mortality in the current study were those which measure physical limitation and inactivity. A pathway from pain to mortality via physical inactivity was strongly supported. This could be through a number of mechanisms as physical inactivity is linked to a wide number of chronic diseases (cardiovascular disease, cancer, diabetes, hypertension, obesity, osteoporosis and depression) (Warburton et al., 2006) (see section 1.6.4). Interventions to increase physical activity in people with pain where possible would help to reduce their risk of mortality by helping to control weight and maintain the function of body systems (Warburton et al., 2006), in addition to reducing the persistence of pain and improving pain related function (Croft et al., 2010).

Table 6.13 Significant mediating factors in each sample from each dataset											
ELSA						**NorStOP**					
Variables	**Complete case**	**Females**	**Males**	**With comorbidity**	**No comorbidity**	**Variables**	**Complete case**	**Females**	**Males**	**With comorbidity**	**No comorbidity**
LIFESTYLE FACTORS											
Physical inactivity	✓	✓	✓	✓	✓	***Current smoking***	✓	X	✓	X	X
Current smoking	X	X	X	✓	X	***Low alcohol consumption***	X	X	X	X	X
Low alcohol consumption	✓	✓	X	✓	X	***Obesity***	X	X	X	X	X
						Low frequency go out	✓	✓	✓	✓	X
						Low frequency walk for 10 minutes	✓	✓	✓	✓	X
						Trouble falling asleep	✓	✓	X	X	X
						Wake in the night	✓	✓	✓	✓	X
						Trouble staying asleep	✓	✓	X	X	X
						Wake up unrefreshed	✓	✓	✓	✓	✓
HEALTH											
Poor self-rated health	✓	✓	✓	✓	✓	***Poor self-rated health***	✓	✓	✓	✓	X
Functional limitation	✓	✓	✓	✓	✓	***Functional limitation***	✓	✓	✓	✓	X
Symptoms preventing walking ¼ mile	✓	✓	✓	✓	✓						
Quality of life (low)	✓	✓	✓	✓	✓						
Control	✓	✓	✓	✓	✓						
Autonomy	✓	✓	✓	✓	✓						
Pleasure	✓	✓	X	X	✓						
Self-realisation	✓	✓	✓	✓	✓						
Allostatic load *	✓	✓	✓	X	X						
Frailty*	✓	✓	✓	✓	✓						

SOCIAL FACTORS										
Low social group membership	✓	X	✓	✓	X	**Social participation restriction**	✓	✓	✓	✓	✓
Volunteer work	✓	✓	✓	✓	X					
PSYCHOLOGICAL FACTORS										
Depression	✓	X	✓	✓	✓	***Anxiety***	✓	✓	✓	✓	✓
Cognitive impairment	✓	✓	✓	✓	✓	***Depression***	✓	✓	✓	✓	X
						Cognitive impairment	✓	✓	✓	✓	✓
						Poor control of health	X	X	X	X	X

✓ Significant mediating factor
✓ Significant mediating factor but with a small indirect effect and confidence interval including 1.00
✓ Significant mediating factor with a Hazard Ratio for the indirect effect of below 1.00
X not a significant mediating factor
* analyses conducted on separate samples with complete biomarker information

Measures of functional limitation resulted in the strongest mediating effects (i.e. resulted in the largest hazard ratios for indirect effects). This is consistent with previous studies reporting reduced functional difficulty in people with pain (Weiner et al., 2003) and associations between functional impairment and mortality (Scott & Macera, 1997). It also supports the work of Docking et al., (2014) who reported increased mortality for women with disabling back pain but no increased risk of mortality in people (men or women) whose back pain was not disabling (Docking et al., 2014).

Self-reported assessments of functional impairment measure perceived limitations in physical capacity rather than the amount of physical activity (Tang et al., 2014) but the former has inevitable consequences for the latter. Functional limitation will lead to physical inactivity and this emphasises the importance of physical capacity and managing functional limitation for people in pain through interventions such as physiotherapy, exercise classes and psychological therapies that address barriers to physical activity (Tang et al., 2014).

Moderating effects

The observed moderating effects of sex and comorbidity for some of the indirect pathways from pain to mortality suggest sub-groups which may respond differently to interventions to reduce mortality risk. However, the moderation analysis should be interpreted with caution due to the reduction in power as a result of the sub-group analysis. The effects observed in the current study were not consistent between the two datasets. Any notable differences between sub-groups (males and females/people with or without comorbidity) are discussed separately for specific mediators in the remainder of this section.

Allostatic load

A small mediating effect of allostatic load was observed in the current study. However, there are a number of limitations regarding this proposed mediator that need to be considered. Debate continues over which grouping of biomarkers optimally represent allostatic load (Gallo, Fortmann, & Mattei, 2014). The constituents of the allostatic load index in this study were determined by the available data; a limitation of secondary data analysis. Another limitation of the measure of allostatic load in this study was that it was measured at one time point only. It therefore does not take into account what would be considered "resting" or "usual" scores on each of the biomarkers for each individual, which an optimal assessment of allostatic load would incorporate (McEwen & Seeman, 1999). Allostatic load refers to an accumulation of maladaptation to stress over time in a number of physiological systems and the need for longitudinal analysis is consistently emphasised in the allostatic load literature but few studies exist (Gallo et al., 2014). A more accurate mediating effect of allostatic load may therefore have been observed in longitudinal analyses measuring change in allostatic load over time. As detailed in Section 4.6, there was insufficient power to conduct analyses examining change over time due to the level of attrition at follow up.

Sex differences in allostatic load have been observed in the biomarkers that make up allostatic load. Neuroendocrine dysregulation is greater in women and cardiovascular system biomarkers show greater dysregulation in men (Beckie, 2012). Therefore different biomarker combinations may result in differences in risk of mortality between men and women rather than any differences in the count of the number of biomarkers.

Interventions to reduce stress by improving sleep quality, social support, self-esteem, sense of purpose, healthy diet and physical activity combined with beneficial practices in

the workplace, cleaner safer neighbourhoods and education may help to reduce allostatic load (Juster, McEwen, & Lupien, 2010) and therefore mortality risk in those with pain.

Frailty

The role of frailty in the relationship between pain and mortality warrants further investigation. People with pain are more likely to be frail than those without pain (Shega et al., 2012), but it may be that frailty is a moderator of the relationship between pain and mortality. Instead of frailty as a result of pain, the risk of mortality for those with pain may be greater for those who are frail than for those who are not frail. Longitudinal analysis is necessary to more accurately determine the role of frailty.

As with all composite measures, interventions to target specific factors within those measures are subsequently likely to result in an improvement in that measure if successful. Interventions to improve the characteristics of frailty (e.g. increase weight, strength, endurance, walking speed and physical activity (Fried et al., 2001)) may reduce the risk of mortality for people with pain.

Depression

The potential difference in the mediated pathways from pain to mortality via depression between males and females is not clear. Sex moderated the relationship via depression in ELSA and NorStOP but in ELSA the effect was in males but not females and in NorStOP the effect was greater in females compared to males. Depression in ELSA was measured using the Centre for Epidemiological Studies depression Scale (CES-D) and in NorStOP the Hospital Anxiety and Depression Scale (HADS) was used. However, these measures are

both screening rather than diagnostic tools for depression, are widely used and validated in different populations (Smarr & Keefer, 2011) and have been shown to measure the same underlying construct and be adequate and equivalent in detecting depression problems (Stafford et al., 2014). As previously stated the reduction in power in the stratified analysis is likely to contribute to the differences in findings between the ELSA and NorStOP datasets. Depression is an important target for intervention in people with pain and the results of this study indicate successful treatment of depression may reduce the risk of mortality in both males and female with pain.

Unexpected findings

a) Alcohol consumption

There was no mediating effect of alcohol consumption in the current study. However, the association between pain and reduced alcohol intake observed in the current study is consistent with previous research (Brennan et al., 2011; McBeth & Nicholl, 2010) and suggests low alcohol consumption may be a proxy for poor health. The symptoms older adults experience, their associated medication use and possibly a subsequent reduction in social activities where alcohol is consumed (Brennan et al., 2011) may explain why pain is associated with lower alcohol consumption.

b) Obesity

The lack of a mediating effect of obesity is surprising considering obesity is associated with an increased risk of mortality (Flegal et al., 2013). BMI has poor sensitivity and specificity as a measure of obesity as it does not take into account age, sex, bone structure, fat distribution or muscle mass (Rothman, 2008). Nonetheless, BMI remains a

commonly used measure of obesity and 23.5% of the NorStOP study sample was classified as obese which is comparable to the national average (26.0% of men and 23.8% of women in 2013) (Health and Social Care Information Centre, 2015). However, people at the lower end of the obesity scale (BMI=30.0-34.9) have been shown to have no increased risk of mortality and those classified as overweight (BMI=25-29.9) demonstrate reduced mortality compared to those of normal weight (BMI=18.5-24.9) (Flegal et al., 2013; Romero-Corral et al., 2006). This study compared people who were obese to those who were not obese so the reference group also included those who were underweight who also have an increased risk of mortality (Flegal, Graubard, Williamson, & Gail, 2005) which may act to dilute any mediating effect of obesity. There may also be some unmeasured factor(s) serving to protect obese people which are successfully reducing their risk of mortality compared to non-obese people. Such factors might include earlier presentation to medical care (Oreopoulos et al., 2009), optimal medication (e.g. statins, blood pressure medication), (Schenkeveld et al., 2012) cardio protective metabolic effects of increased body fat (Hastie et al., 2010) and benefits of higher metabolic reserves (Doehner, Clark, & Anker, 2010) which may be particularly important in older people.

c) Sleep

There was an increase in the direct effect compared to the total effect of 'waking up unrefreshed' in participants without comorbidity in the NorStOP sample which indicated a suppressing effect (where the magnitude of a relationship becomes larger with the inclusion of a third variable) (MacKinnon, Krull, & Lockwood, 2000). This should be interpreted with caution due to the small sample size of this group. This study measured pain and sleep problems at the same time point so it was not possible to determine which

came first, however, sleep is an important target for health interventions in people with pain as restorative sleep has been shown to predict the resolution of chronic widespread pain after 15 months (Davies et al., 2008). This study indicates successful interventions to improve sleep may also reduce mortality risk for people with pain.

d) Smoking

In NorStOP the observed mediating effect of smoking suggested that being a current smoker was protective for males with any pain. Smoking is consistently associated with an increased risk of all-cause mortality in older people (Gellert et al., 2012) therefore the finding for males in the current study is unusual. However, the extent of mediation is small. The dichotomy of current smoker/non-smoker used in this analysis is a limitation as it only measures current smoking status. Mortality from smoking is linked to the number of cigarettes smoked and to when people stopped (Doll et al., 2004), and this comparison between never/previous smokers and current smokers does not provide an account of this. It may be more likely that a current smoker with pain may increase the amount they smoked as a way to cope with their pain (Ditre & Brandon, 2008); however this hypothesis could not be tested in this study. It was also not possible to test the direction of the relationship between pain and smoking. Pain may be associated with not being a current smoker as a result of other health conditions prompting an individual to quit, and those other health conditions may account for the increased risk of mortality in those people. However, there was also an indirect effect of not being a current smoker in those without comorbidity in the NorStOP sample but there was insufficient power to detect an effect in this group (only n=1984 people indicated they did not have any comorbidities and only 107 died resulting in power of only 27.33% to detect a hazard ratio of 1.3).

6.7.3 Interventons to reduce mortality risk

The mediating factors identified in this study such as physical activity, physical function, sleep and depression are all factors which are already targeted in pain management (Main et al., 2007). The purpose of the current study was to demonstrate and explain the potential long term consequences for people with pain rather than identify novel targets for intervention. The mediating factors identified are modifiable and as such an improvement in those factors could act to reduce the risk of mortality for people with pain. The mediators in this study were assessed individually but factors such as depression, sleep, allostatic load and frailty overlap and interventions to improve one of these factors may also act to improve others. The implications of the current study for practice are discussed further in section 7.4.

6.7.4 Comparison with other studies

This was the first study to investigate potential mediators of a relationship between pain and mortality, and one of only a small number of studies that have examined mediating effects within survival analysis. Andersson (2009) reported an association between widespread pain and mortality that was explained by lifestyle factors; specifically smoking, physical activity, stress and sleep disorders (Andersson, 2009). However, Andersson's study did not test pathways from pain to mortality; factors were adjusted for as confounders within survival analysis. In the current study physical inactivity, stress (measured by allostatic load, anxiety and depression) and sleep problems were all shown to be significant mediators of the relationship between pain and mortality which both supports and adds to Andersson's findings. However, smoking was not shown to be

associated with pain in this study. This may also in part account for the lack of association between pain and cancer mortality reported in Chapter Five.

6.7.5 Methodological considerations

Dichotomising

The method used to undertake the mediation analysis within survival analysis is an emerging technique, and the R code used to perform the analysis can currently only calculate outcomes using dichotomous predictors and mediators. It was therefore necessary to dichotomise these variables. This is a major limitation of this study. Dichotomising results in a loss of information, particularly for continuous variables where dichotomising treats some scores that are almost indistinguishable i.e. those near the cut point, as though they are distinct from each other (Altman & Royston, 2006; Streiner, 2002). All observed values in a study incorporate some measurement error and for individuals near a cut point this measurement error may result in misclassification into the wrong group rather than just an inaccurate score (Streiner, 2002). Approximately one-third of information is lost as a result of dichotomising variables resulting in a loss of power to detect an existing effect (Altman & Royston, 2006; Royston, Altman, & Sauerbrei, 2006).

Dichotomisation can result in a loss of effect size and statistical significance when examining bivariate relationships but spurious statistical significance and an overestimation of effect size in analyses where there are two independent variables (MacCallum, Zhang, Preacher, & Rucker, 2002). Relationships that are not linear also

have the potential to be overlooked when variables are dichotomised (MacCallum et al., 2002).

The cut-off to determine where to dichotomise a variable is often arbitrarily determined and produces groups that are not psychometrically meaningfully (i.e. reliable, repeatable, valid measures) (Hayes, 2013). For example, the median is often used to determine the cut point when dichotomising which means different studies will use different cut points based on their sample medians therefore cannot be compared (Altman & Royston, 2006; Royston et al., 2006). However, dichotomising may be justifiable in cases where prior analyses provide clear support for the existence of two groups with a clearly identifiable scale point differentiating the groups, or where the data is highly skewed and there are a large number of scores at the most extreme end of the distribution (MacCallum et al., 2002; Streiner, 2002).

Table 6.13 summarises all statistically significant mediating factors in the current study but also highlights those factors where the hazard ratio for the indirect effect is close to 1.00. The loss of information as a result of dichotomising reduces confidence these variables are true mediators of the relationship between pain and mortality.

Multiple testing

When multiple hypotheses are considered simultaneously (as in this study) the probability of falsely detecting a significant effect where there isn't one increases with each additional test performed (Bender & Lange, 2001). It was not possible to correct for this potential problem in the current analyses. This is commonly done by adjusting the p-values or confidence intervals to account for the number of tests run (Sainani, 2009).

Further development of the method to undertake mediation analysis within survival analysis should enable this to be possible in future studies using this technique. However, although adjusting the criterion for significance in this way reduces the risk of a type I error (false –positive) it increases the risk of type II error (not finding an existing effect) (Rothman, 1986). Often datasets are used to test many hypotheses, but these are reported in separate papers and adjustment for the number of tests is not performed as each individual hypothesis is examined as the sole focus of a study (Rothman, 1986). Although many tests were performed in this thesis, all results are presented and statistically significant findings should be interpreted as suggestive only (Rothman, 1986). Effect sizes should be taken into consideration, that is, larger effect sizes are less likely to be chance findings and where findings are replicated in different data samples (such as with the mediating/indirect effects of the functional limitation and physical inactivity measures in this study) there can be more confidence about the true existence of those effects (Sainani, 2009). Adjustment for multiple testing is more important when the results of the multiple tests are combined in one final conclusion or decision (Bender & Lange, 2001) which was not the case in this thesis.

Self-report

Most of the variables in this study were measured using self-report methods. Information obtained by self-report is limited by inaccuracies due to problems with recall and with differing interpretations of questions which affects face validity. A particular example of this is with the report of physical activity levels in the ELSA dataset. A high proportion of the sample (31.04%) reported engaging in vigorous activities at least once a week. This could be a result of information bias; one person's idea of what constitutes vigorous

activity may differ greatly from another person's opinion, recall bias where an inaccurate recollection of activity is reported or response bias where participants provide what they perceive to be more favourable answers (e.g. higher activity levels) (Delgado-Rodríguez & Llorca, 2004). Or it may indeed be that the ELSA sample is in fact an active group of older adults (as has been reported elsewhere (Lang, Guralnik, & Melzer, 2007)).

Overlapping measures

There will also be overlap between some of the variables used in this study with regards to the constructs being measured. Of note are the moderating effects of comorbidity in the NorStOP analyses. The method used to capture morbidities in NorStOP is likely to measure some of the same elements captured by the variables 'frequency go out', 'frequency walk for 10 minutes', 'self-rated health', 'anxiety' and 'depression', where a significant moderating effect of comorbidity was observed. However, measuring these items separately (i.e. as moderator and individual mediators) allows a more detailed investigation of how and in whom pathways from pain to mortality exist. Indirect pathways from pain to mortality were observed in participants both with and without comorbidity indicating that interventions to target identified mediating factors are important to reduce mortality risk in everyone with pain, not just in those with comorbidity.

Use of single items

This study used a number of single items to measure potential mediators. The use of a single item is limited compared to multi-item measures as it is difficult to capture multi-dimensional concepts using just one question. The information ascertained from a single

item lacks detail if the targeted concept is broad (i.e. health status). Multi-item measures are considered more reliable, stable and precise and they are likely to produce more consistent responses and are less prone to sociopsychological biases (e.g. response bias) (Bowling, 2005).

An example of this in the current study was the attempt to measure 'control'. The lack of a significant indirect effect of perceived control in NorStOP may be due to inadequacy of the single item used to accurately capture the concept of control. A comparison could be made between the item used from the IPQ-R in NorStOP and the control domain from the CASP-19 that was used in the ELSA dataset (which did mediate the relationship between being often troubled with pain and mortality). The item from the IPQ-R attempted to capture an individual's belief over their ability to control their health whereas the control domain of the CASP-19 attempts to capture the ability to actively intervene in one's environment (Hyde et al., 2003). A control-positive domain (i.e. positive feelings of control) from the Aging Perceptions Questionnaire (APQ) (developed from the IPQ-R) has been shown to have a weak association with the control/autonomy domains of quality of life measured using the CASP-R12 (developed from the CASP-19) (Sexton, King-Kallimanis, Morgan, & McGee, 2014). It is likely therefore these are measuring different constructs which would explain the difference in findings. Control may be useful as a direct target for intervention but similar to the quality of life measure, it is also likely to be influenced by interventions to improve other factors (e.g. depression, functional limitation).

Advantages of the use of single items include ease of administration, interpretation and reduced costs (Bowling, 2005). The single-item self-reported health measure (a version of which was used in each of the datasets in this study) has been acknowledged as a robust

measure of health status following application in a large number of population surveys (Bowling, 2005; Chandola, Tarani, Jenkinson, 2000). Other single item measures were used to capture narrower concepts (e.g. individual sleep items) which provide information about more precise targets for intervention. The use of single items therefore has advantages and disadvantages and these should be considered in the interpretation of results using these items.

Composite measures

Measures which capture broad constructs such as general health and quality of life may not be direct targets for intervention but would be influenced by the management of other targets. Consideration must be given to what is actually being measured in the assessment of self-rated health for example, as it is a concept which encompasses a number of domains. Improvements in self-rated health are therefore likely to be dependent on a broad range of factors. Self-rated health is a measurement of the presence of illnesses, symptoms, beliefs about severity, family influences, past and current health (Idler & Benyamini, 1997; Jylhä, 2009). It also overlaps with concepts such as quality of life. When people rate concepts such as health or quality of life they conduct an appraisal process which involves 1) the induction of a frame of reference they deem relevant based on their understanding of the question, 2) the recall and sampling of salient experiences which are 3) judged against standards of comparison. These may be based on personal reference points such as prior functioning and lost capabilities or on observations of others, past experiences with illnesses or external communication from healthcare providers. 4) Individuals then use a subjective algorithm to combine these appraisals and experiences into their response to the question (Rapkin & Schwartz, 2004).

Interventions to improve the individual lifestyle, health, social and psychological factors indicated as mediators in this study are likely to subsequently result in improved quality of life/self-rated health ratings in addition to reduced mortality risk.

Sub-group analysis

Despite having previously been recommended as an approach to assess moderation in mediation analysis (Reis & Judd, 2000) and in structural equation modelling (Rigdon, Schumacker, & Wothke, 1998), analysing sub-groups separately has a number of limitations. Each sub-group will have lower statistical power than the full sample and sub-group analysis does not provide significance tests of differences in mediation across levels of the moderator variable (Edwards & Lambert, 2007). As described above, the method to undertake mediation analysis within survival analysis used in this study is an emerging technique. Further development of the technique and the statistical packages used to perform the analyses is necessary to enable the use of non-binary variables and allow for multiple group comparisons which would mean more comprehensive models could be tested, including moderated mediation models (see section 7.3).

6.7.6 Strengths and limitations

This study has a number of strengths. This is the first study to use mediation analysis to examine potential mechanisms for a relationship between pain and mortality. A cutting-edge technique was used to estimate the extent of mediation by the proposed mediators within survival analysis accounting for time. The study was conducted in two large population surveys which provided adequate total sample sizes to detect the predicted effects and enabled a number of factors to be investigated as potential mediators of the

relationship between pain and mortality. Key targets and potential subpopulations were identified to reduce mortality in older adults with pain.

A single mediator cannot fully explain a relationship between an exposure and outcome but testing individual mediators helps to determine which different factors may contribute to a more complex relationship. In the analysis undertaken in this study from the ELSA dataset, pain described as “often troubling” continued to have a significant direct effect on mortality in some of the mediation models. This description of pain may capture a number of different ways pain impacts on an individual’s life and the individual mediators examined account for only some of this impact. In the NorStOP analyses, the report of “any pain” did not have a significant direct effect on mortality, therefore the significant mediators identified in the NorStOP analyses help to confirm how pain impacts on an individual and subsequently leads to increased mortality. Where similar mediators were measured in each dataset, those with stronger mediating effects in the ELSA dataset were the same mediating factors that had significant indirect effects in the NorStOP dataset (e.g. poor self-rated health, physical inactivity, functional limitation). This implies these findings were not a result of chance.

Limitations of mediation analysis are discussed further in section 7.3 but most notable is the need for longitudinal data. Mediation analysis is carried out in an attempt to elucidate mechanisms for relationships between exposures and outcomes. Often, as in this study, mediators are considered individually and have been measured at the same time as the exposure. Causal inference based on observational data, particularly cross-sectional data should be made with caution (Grimes & Schulz, 2002).

6.7.7 Implications for research and practice

This study has identified a number of factors that explain the relationship between pain and mortality and are potential targets for reducing the risk of death. Further development of the technique used to undertake the mediation analysis would allow for a more detailed and precise investigation of mediating factors, particularly with categorical and continuous variables. This would provide a more accurate representation of the relationships investigated in this study. However, this study has provided a strong indication that factors affecting mobility, physical activity and perception of health are important mediators of the relationship between pain and mortality. Interventions to increase physical function, physical activity and perceived general health may help to reduce the risk of death in those with pain.

6.8 Key messages

- Physical inactivity, functional limitation and self-rated health were notable mediators of the relationship between pain and mortality.
- Indirect pathways from pain to mortality were evident in the absence of a total effect.
- Sex and comorbidity were indicated as potential moderators for some of pathways between pain and mortality.
- Further development of the technique to undertake mediation analysis within survival analysis is imperative to provide a more precise description of the relationships indicated by this study.

Chapter Seven. Discussion

7.1 Thesis summary

This thesis presents the results of a large population based study of the relationship between pain and mortality. A systematic review of the current literature identified ten studies which had investigated the relationship between pain and mortality. These studies had differing population characteristics, methods of analysis and included different covariates and pain phenotypes which prevented clear conclusions from being drawn. The current study added to existing work by examining how the classification of pain, i.e. the pain phenotype, impacted on the relationship between pain and mortality and expanded the investigation of the role of covariates by assessing whether they mediated or moderated the relationship. A detailed interpretation of the analyses undertaken in this thesis are presented in Chapters Five and Six and here a summary of the key points are presented to critically re-evaluate notable findings and implications for research and practice.

7.2 General discussion

7.2.1 Summary of findings

The analysis in this thesis reported that in support of previous studies people with pain had an increased risk of mortality, pain that had an impact on daily life was an important predictor of death rather than the presence of pain *per se*, and suggested that important mechanisms from pain to mortality were functional limitation and physical inactivity.

7.3 Implications for research

This was the first study to formally test potential mechanisms of a relationship between pain and mortality. A novel technique to conduct mediation analyses within a survival model was undertaken. Important points to consider in the interpretation of the findings are detailed below.

7.3.1 Mediation analysis

Multiple mediators

This study identified factors that mediated and could explain the relationship between pain and mortality. There are a number of important caveats to that observation. A single mediator is unlikely to act in isolation and may instead be part of a longer "causal pathway" that includes many potential mediators. For example pain is associated with a reduction in physical activity (McBeth & Nicholl, 2010), which in turn may increase the risk of depression (Teychenne, Ball, & Salmon, 2008) and subsequent death (for example through hazardous health behaviours, suicide or an interference with motivation for recovery) (Cuijpers & Smit, 2002). A number of factors may also contribute simultaneously to a reduction in health and subsequent mortality (parallel mediation) (Hayes, 2013). Studying mediators individually does not inform us of the relative influence of a number of different mediators.

Longitudinal analysis

In order to study potential causal chains longitudinal analysis is needed. Hill (1965) specified criteria to be considered to determine whether an association is causal; 1) the strength of the association, 2) the consistency of the association (replicable), (3)

specificity (the cause leads to a single, not multiple effects), 4) temporality (the cause precedes the effect), 5) biological gradient (a dose-response effect), 6) plausibility (makes sense biologically), 7) coherence (consistent with what is already known), 8) experimental evidence (involving the manipulation of variables) and 9) analogy (similar relationships have been observed elsewhere) (Hill, 1965). Although the current study fulfilled some of these criteria the mediation analyses did not meet criterion 4) which is indisputable (in the current study the predictor and mediator were measured at the same time point); if the cause does not precede the effect then the association cannot be causal (Rothman, 1986) and longitudinal analysis is necessary to determine temporality.

Although the current study used data from longitudinal studies it was not possible to use the data at different time points for the mediation analyses due to attrition. The power analysis conducted in Chapter Four indicated sufficient power (86.35%) to detect a HR of 1.4 in the NorStOP follow up sample, but the observed effect size was only HR 1.05 (95%CI 0.94, 1.18) in the complete case sample (n=10985). The power to detect an effect of this size in the follow-up sample for NorStOP (n=4293) was only 6.47%. It was therefore not possible to conduct mediation analyses including change scores over time in this study.

Alternative explanations

Mediator and moderator analyses are based on theoretical events or processes that unfold over time and the sequence is determined by what is theoretically plausible. However, there are often multiple ways of defining the relationships between the variables (Roe, 2012). Many relationships are reciprocal (e.g. pain and depression (Chou, 2007), pain and sleep problems (Moldofsky, 2001)). In reality, models of relationships

between variables are non-recursive, that is, they involve feedback loops, but these models are problematic to test (Streiner, 2005). The pathways between pain and mortality identified by the current study are useful for suggesting potential targets for intervention but the true complexity of relationships and processes can never be modelled exactly using statistical techniques. The use of longitudinal analysis and a combination of quantitative and qualitative methods would help to support and clarify the mediational processes suggested by this study (Mackinnon, Fairchild, & Fritz, 2007).

7.3.2 Mediation analysis within survival analysis

Current limitations

The analysis performed in this thesis was greatly restricted by the requirement to use only dichotomous variables for the mediation analysis due to the limitations in the novel technique employed. The assessment of categorical/continuous mediators would provide a more accurate and precise evaluation of the relationships involved by overcoming the problems associated with dichotomising (discussed in section 6.7.4).

Assessing moderation

It was possible to include interaction terms in the survival models (presented in Appendix VI) which revealed no significant moderating effects of sex or comorbidity on the relationship between any of the pain phenotypes and mortality. However, it was not possible to include interaction terms in the mediation models. Moderated mediation was therefore tested by stratifying the mediation analyses and describing the differences between the groups observing where confidence intervals did not overlap (presented in Chapter Six). A more accurate way of assessing moderated mediation would have been to

perform multiple group analysis. This was not possible in the current study. Multiple group analysis is a statistical technique which analyses groups simultaneously, provides more accurate parameter estimates than sub-group analyses and tests for statistically significant differences between groups (Arbuckle, 2012). Further development of statistical packages and techniques to conduct mediation analysis within survival analysis are necessary to allow categorical and continuous variables to be entered into the models, to allow for multiple group comparisons to be undertaken assessing moderated mediation models and to include model fit statistics to indicate how well the models fit the data.

7.3.3 Secondary data analysis

Established datasets such as ELSA and NorStOP provide scope for researching a number of issues relating to the health and lives of older adults; they are large databases which have data on a broad range of factors. Using such data increases cost efficiency and reduces the amount of time necessary to undertake research. However, the questions that can be asked on a particular topic are restricted by the available data. Secondary data analyses are unlikely to be ideal for answering research questions compared to if the database had been designed specifically to answer those proposed questions. For example, in order to optimally investigate mediation, the predictor variables should be measured before the mediator which in turn should be measured before the outcome (Kline, 2015). Baseline measures of the mediator and outcome variable are also necessary (where possible) to control for those values in order to isolate the effect of the proposed mediator (Keele, 2015). Also, the intervening time intervals should be appropriate (i.e.

not too long and not too short) to allow for a measureable change to have occurred (Mathieu & Taylor, 2006).

Measurement issues

The way in which factors are measured in an existing dataset may not be optimal to answer the research questions of a proposed study and may not be comparable to other studies. For example, in the current study the measures of physical activity from both the ELSA and NorStOP databases had limitations. ELSA asked participants how often they took part in mild, moderate or vigorous activity. This is potentially limited by the subjective interpretation of what 'mild', 'moderate' or 'vigorous' activity constitutes and by reporting bias where the participants may specify greater activity as this is seen as socially desirable. A high proportion of ELSA participants (31.04% ELSA) reported weekly vigorous activity. Mean percent differences between subjective and objective measures of physical activity are greater when activity is categorised by levels of exertion with differences becoming greater with higher categories of intensity (i.e. participants indicate higher levels of vigorous activity when using self-report) (Prince et al., 2008). Misclassification of activity levels in the current study was therefore likely but the impact of this misclassification is unclear due to the need to dichotomise variables for the analysis. The resulting loss of information means the interpretation of the mediating effect of physical inactivity lacks detail. This is also true of the NorStOP measures of activity; 'frequency of going out' and 'frequency of walking for 10 minutes'. 'Going out' does not necessarily reflect physical activity and although walking for 10 minutes does detail the type and duration of the activity, it is only one form of activity the participant may undertake and may be performed at varying levels of intensity (e.g. briskly or leisurely). In order to get a

more accurate representation of activity levels and the effect these may have on the relationship between pain and mortality objective measures such as pedometers or accelerometers could have been used to validate the reports of physical activities undertaken. However, these again are limited as they do not monitor activities such as swimming or upper body activities (Prince et al., 2008). The current study provides little information on the amount or type of physical activity that would be beneficial in reducing mortality risk in people with pain. Despite the limitations of different methods of measurement, designing a dataset with specific research questions in mind would enable a more valid and comprehensive assessment of the factors under investigation, provided the analysis technique used could accommodate the measures.

7.3.4 Generalisability of findings

This study provides evidence for a relationship between pain and mortality and identified potential mechanisms for that relationship. There were differences between the two samples used in the current study but the mediating effects of functional limitation, physical inactivity and poor self-rated health resulted in large effect sizes and was replicated in two different datasets. Data from ELSA is harmonised with data from other studies of ageing populations around the world (www.g2aging.org). These studies have common measures across surveys which would enable future replication attempts of the analyses from the current study. This would provide opportunities for cross national comparisons and the investigation of the effect of different national and policy contexts on the relationship between pain and mortality to determine if the relationships observed were generalisable (Chan et al., 2012).

7.4 Implications for practice

The high prevalence of pain means the risk of mortality affects a large number of people. A population approach to the management of pain may be effective in reducing the population burden with respect to mortality. The effective treatment of pain itself is not always possible; the source of pain (e.g. serious injury) may not be treatable; symptoms often do not resolve; and pain trajectories may be stable over time, persons with persistent back pain have been shown to remain in the same trajectory (recovering, persistent mild, fluctuating and severe chronic) over 7 years (Dunn, Campbell, & Jordan, 2013). There is a need instead to minimise the negative consequences of pain and this study identified a number of potential targets for interventions.

7.4.1 Interventions to reduce mortality risk

The findings from the current study indicate interventions targeted at improving functional capacity and increasing physical activity are particularly important for reducing mortality risk in people with pain. Increasing functional capacity and physical activity levels is difficult in people with pain; activity may increase the pain experienced by the individual (Soldato et al., 2007) or the reasons for inactivity may be as a result of disability (McGuire, Strine, Okoro, Ahluwalia, & Ford, 2007). In a systematic review Jack et al., (2008) reported lower previous activity levels, low-self-efficacy, depression, anxiety, poor social support or activity, greater perceived number of barriers to physical activity and increased pain levels during exercise were barriers to treatment adherence in physiotherapy outpatient clinics. They also acknowledged their review included a range of musculoskeletal conditions and that barriers may vary according to condition and population (Jack, McLean, Moffett, & Gardiner, 2010). The findings from the current study

suggest that if improvement in one target is not realistically achievable (i.e. an increase in physical activity) other target areas (i.e. depression, social participation) could be focussed upon which would also help to reduce mortality risk for people with pain. Interventions to reduce mortality risk for people with pain should also aim to reduce medication use; a recent study in Denmark demonstrated long term opioid use was associated with a greater increased risk of mortality than short-term or no opioid use in participants with chronic non-cancer pain compared to those with no chronic pain (Ekholm, Kurita, Hjsted, Juel, & Sjgren, 2014).

7.4.2 Obstacles to effective pain management

Many of the mediating factors identified in the current study are already targeted in pain management programmes to improve health outcomes. However, pain is inadequately treated as a result of cultural, attitudinal, educational, legal and political system related reasons (Brennan, Carr, & Cousins, 2007). For example, patients often do not challenge health professionals and patients with chronic non-cancer pain can be seen as malingerers or be deemed to have only psychological problems (Brennan et al., 2007). The co-ordinated integration of medical, psychosocial, and physical treatment in interdisciplinary care offers the best clinical care for the individual with pain and is a cost effective option for long term treatment (Gatchel, McGeary, McGeary, & Lippe, 2014). However, the up-front costs and the complexities of creating an interdisciplinary service mean this type of treatment is a resource that is available to only a few of those who may benefit (Gatchel et al., 2014). In an interview survey with 504 General Practitioners (GPs) in the UK about the management of chronic non-malignant pain, 91% of GPs considered specialised pain services to be beneficial but only 14% of patients were referred to

hospital for symptom management, 96% felt that pain services in their locality could be improved and 81% expressed an interest in relevant training (Stannard & Johnson, 2003). This indicates scope for the improvement of pain services.

There is evidence that mortality risk for people with pain could be reduced with effective pain management. In a thirteen year follow up of chronic pain patients in a pain management programme in the United States, Maruta et al., (1998) found the survival of the patients to be virtually identical to that of the general US population. Patients in this study were required to have a pain problem of six months duration or longer. The programme was designed to help patients and family members cope effectively, help patients reduce medication to a minimum and teach self-management methods (Maruta et al., 1998). The findings of this thesis provide supporting evidence that at a population level, mortality risk for people with pain could be reduced by the effective management of pain and its impact.

7.5 Concluding messages

- People with pain which impacted on their life had an increased risk of mortality.
- Pain was not associated with any specific cause of mortality.
- The relationship between pain and mortality was dependent on pain phenotype.
- Physical inactivity, functional limitation and poor self-rated health were indicated as important mediators of the relationship between pain and mortality but many factors were identified as potential targets to reduce mortality risk.
- There were differences between males and females in the mediated pathways from pain to mortality and between those with and without comorbidity which warrant further investigation.

- Development of the statistical techniques to undertake mediation analysis within survival analysis is necessary to enable a more detailed investigation of relationships using this form of analysis.

List of publications and presentations

Publications:

Smith, D., Wilkie, R., Uthman, O., Jordan, J.L. & McBeth, J. (2014) *Chronic Pain and Mortality: A Systematic Review*. PLOS ONE, vol. 9(6), Article ARTN e99048

Sibille, K.T., McBeth, J., Smith, D. & Wilkie, R. (pending) *Allostatic load and pain severity in older adults: Results from the English Longitudinal Study of Ageing*. Submitted to Experimental Gerontology

Presentations:

Smith, D., Wilkie, R., McBeth J. (2012) *Widespread pain and mortality*. Oral presentation: Primary Care Sciences Research Symposium, Keele University

Smith, D., Wilkie, R., Uthman, O., Jordan, J.L., McBeth J. (2013) *Widespread pain and mortality – a systematic review and meta-analysis*. Poster presentation: British Pain Society Annual Scientific Meeting, Bournemouth

Smith, D., Wilkie, R., McBeth J. (2014) *The relationship between pain and mortality is mediated by frailty*. Poster presentation: British Pain Society Annual Scientific Meeting, Manchester

Smith, D., Wilkie, R., McBeth J. (2014) *The relationship between pain and mortality is mediated by frailty*. Oral presentation: Primary Care Sciences Research Symposium, Keele University

Smith, D., Wilkie, R., McBeth J. (2014) *Pain and mortality in older people: mediation by psychological, physical and physiological stress*. Poster presentation: International Association for the Study of Pain World Congress, Buenos Aires

Smith, D. (2015) *A study of pain and mortality: the role of lifestyle, health, social and psychological factors.* Oral presentation: UKRiME, Manchester

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Appendix I - Full search strategy

MEDLINE using OVID SP (1946 to present)

1	mortality.ti,ab.	380773
2	mortality/	31524
3	cause of death/	31017
4	fatal outcome/	43948
5	hospital mortality/	17629
6	"cause of death".ti,ab.	31705
7	fatal*.ti,ab.	89282
8	death.ti,ab.	389950
9	death/	10928
10	death,sudden/	10434
11	dead.ti,ab.	32464
12	died.ti,ab.	165667
13	survival/	3445
14	survival.ti,ab.	485299
15	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	1296926
16	(widespread adj3 pain).ti,ab.	979
17	arthralgia.ti,ab.	3547
18	fibromyalgia.ti,ab.	5476
19	myalgia.ti,ab.	4138
20	(chronic adj3 pain).ti,ab.	29541
21	(joint adj pain).ti,ab.	3430
22	(radicular adj pain).ti,ab.	1362
23	(regional adj3 pain).ti,ab.	2046
24	"presence of pain".ti,ab.	630
25	(mult* adj3 pain).ti,ab.	3132
26	(comorbid* adj3 pain).ti,ab.	376
27	musculoskeletal pain/	81
28	chronic pain/	281
29	exp joint pain/	5916
30	fibromyalgia/	5322
31	pain measurement/	50607
32	"non* cancer pain".ti,ab.	291
33	"non* malignant pain".ti,ab.	239
34	pain/mo	70

35	arthralgia/	3670
36	complex regional pain syndromes/	676
37	myofascial pain syndromes/	1079
38	((NECK or CERVICAL) adj3 PAIN).ti,ab.	6779
39	((KNEE* or HIP or HIPS or SHOULDER*) adj3 PAIN).ti,ab.	10990
40	((FOOT or FEET or ANKLE* or ELBOW*) adj3 PAIN).ti,ab.	2364
41	((MUSCULO* or MUSCULAR) adj3 PAIN).ti,ab.	3624
42	((BACK or LUMBAR or LUMBO* or SPINE or SPINAL) adj3 PAIN).ti,ab.	29792
43	Back Pain/mo [Mortality]	9
44	Shoulder Pain/mo [Mortality]	1
45	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44	132018
46	Longitudinal Studies/	68770
47	Cohort Studies/	129164
48	Prospective Studies/	310346
49	Family Practice/ or General Practice/	59151
50	Retrospective Studies/	403154
51	Case-Control Studies/ or Epidemiologic Methods/	170484
52	Cross-Sectional Studies/	134718
53	"family pract*".ti,ab.	8324
54	"general pract*".ti,ab.	54841
55	(observ* or cohort or prospectiv* or retrospectiv* or population or longitud* or community or case* control or cross* section*).ti,ab.	3556111
56	46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55	3957958
57	15 and 45 and 56	2342
58	limit 57 to (english language and humans)	**1935**

EMBASE using OVID SP (1980 to present)

1	mortality.ti,ab.	455842
2	mortality/	400684
3	cancer mortality/	40133
4	standardized mortality ratio/	470
5	"cause of death".ti,ab.	38288
6	exp cause of death/	54041
7	death.ti,ab.	454083
8	death/ or fatality/	143765

9	dead.ti,ab.	36715
10	sudden death/	30665
11	died.ti,ab.	191213
12	fatal*.ti,ab.	101502
13	survival/	130224
14	survival.ti,ab.	571242
15	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	1668788
16	(widespread adj3 pain).ti,ab.	1352
17	fibromyalgia/	10368
18	chronic pain/	25260
19	arthralgia/	28014
20	arthralgia.ti,ab.	4703
21	pain assessment/	53996
22	fibromyalgia.ti,ab.	7996
23	myalgia/	27190
24	myalgia.ti,ab.	5341
25	(chronic adj3 pain).ti,ab.	39396
26	exp musculoskeletal pain/	3051
27	(joint adj pain).ti,ab.	4397
28	radicular pain/	1671
29	(regional adj3 pain).ti,ab.	3222
30	(radicular adj pain).ti,ab.	1724
31	"presence of pain".ti,ab.	802
32	(mult* adj3 pain).ti,ab.	4492
33	(comorbid* adj3 pain).ti,ab.	520
34	"non* cancer pain".ti,ab.	477
35	"non* malignant pain".ti,ab.	375
36	complex regional pain syndrome/	1807
37	myofascial pain/	6245
38	((NECK or CERVICAL) adj3 PAIN).ti,ab.	8353
39	((KNEE* or HIP or HIPS or SHOULDER*) adj3 PAIN).ti,ab.	13404
40	((BACK or LUMBAR or LUMBO* or SPINE or SPINAL) adj3 PAIN).ti,ab.	37797
41	((FOOT or FEET or ANKLE* or ELBOW*) adj3 PAIN).ti,ab.	2952
42	((MUSCULO* or MUSCULAR) adj3 PAIN).ti,ab.	4840
43	hip pain/ or low back pain/ or spinal pain/ or foot pain/ or ankle pain/ or bone pain/ or knee pain/ or shoulder pain/ or neck pain/	59850
44	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43	229400
45	prospective study/	183136

46	cohort analysis/	109928
47	population research/	55964
48	longitudinal study/	48485
49	observational study/	26687
50	community assessment/	1090
51	general practice/	62244
52	retrospective study/	251160
53	case control study/	57709
54	cross-sectional study/	63425
55	"family pract*".ti,ab.	8406
56	"general pract*".ti,ab.	65835
57	(observ* or cohort or prospectiv* or retrospectiv* or population or longitud* or community or case* control or cross* section*).ti,ab.	4024951
58	45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57	4238696
59	15 and 44 and 58	5684
60	limit 59 to (human and english language)	**4651**

AMED using OVID SP (1985 to present)

1	mortality.ti,ab.	1718
2	Mortality/	776
3	Death/	1564
4	"cause of death".ti,ab.	235
5	death.ti,ab.	4905
6	fatal outcome/	4
7	Death sudden/	41
8	dead.ti,ab.	207
9	died.ti,ab.	1176
10	survival.ti,ab.	1982
11	fatal*.ti,ab.	305
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	9383
13	(widespread adj3 pain).ti,ab.	206
14	Arthralgia/	100
15	arthralgia.ti,ab.	39
16	fibromyalgia/	1448
17	fibromyalgia.ti,ab.	1542
18	myalgia.ti,ab.	61
19	(chronic adj3 pain).ti,ab.	3521

20	(joint adj pain).ti,ab.	195
21	(radicular adj pain).ti,ab.	64
22	complex regional pain syndromes/	28
23	(regional adj3 pain).ti,ab.	183
24	"presence of pain".ti,ab.	52
25	(mult* adj3 pain).ti,ab.	500
26	(comorbid* adj3 pain).ti,ab.	41
27	Pain measurement/	806
28	"non* cancer pain".ti,ab.	17
29	"non* malignant pain".ti,ab.	21
30	Myofascial pain syndromes/	230
31	((NECK or CERVICAL) adj3 PAIN).ti,ab.	1252
32	((KNEE* or HIP or HIPS or SHOULDER*) adj3 PAIN).ti,ab.	1602
33	((FOOT or FEET or ANKLE* or ELBOW*) adj3 PAIN).ti,ab.	620
34	((BACK or LUMBAR or LUMBO* or SPINE or SPINAL) adj3 PAIN).ti,ab.	5461
35	((MUSCULO* or MUSCULAR) adj3 PAIN).ti,ab.	674
36	Low back pain/ or Backache/	5091
37	shoulder pain/	183
38	Neck pain/	705
39	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38	13771
40	cohort studies/ or prospective studies/	622
41	Family practice/	803
42	epidemiologic methods/	479
43	"family pract*".ti,ab.	132
44	"general pract*".ti,ab.	1149
45	(observ* or cohort or prospectiv* or retrospectiv* or population or longitud* or community or case* control or cross* section*).ti,ab.	40041
46	40 or 41 or 42 or 43 or 44 or 45	41539
47	12 and 39 and 46	**42**

PSYCHINFO using OVID SP (1802 to present)

1	mortality.ti,ab.	19078
2	Mortality Rate/	4561
3	"cause of death".ti,ab.	2333
4	"Death and Dying"/	19022
5	fatal*.ti,ab.	6614

6	death.ti,ab.	48028
7	dead.ti,ab.	3838
8	died.ti,ab.	8193
9	survival.ti,ab.	20460
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	95102
11	(widespread adj3 pain).ti,ab.	286
12	arthralgia.ti,ab.	47
13	fibromyalgia.ti,ab.	1787
14	myalgia.ti,ab.	150
15	(chronic adj3 pain).ti,ab.	10512
16	(joint adj pain).ti,ab.	264
17	(radicular adj pain).ti,ab.	64
18	(regional adj3 pain).ti,ab.	481
19	"presence of pain".ti,ab.	150
20	(mult* adj3 pain).ti,ab.	1357
21	(comorbid* adj3 pain).ti,ab.	205
22	"non* cancer pain".ti,ab.	103
23	"non* malignant pain".ti,ab.	81
24	Myofascial Pain/	255
25	((NECK or CERVICAL) adj3 PAIN).ti,ab.	764
26	((KNEE* or HIP or HIPS or SHOULDER*) adj3 PAIN).ti,ab.	521
27	((FOOT or FEET or ANKLE* or ELBOW*) adj3 PAIN).ti,ab.	104
28	((BACK or LUMBAR or LUMBO* or SPINE or SPINAL) adj3 PAIN).ti,ab.	3806
29	((MUSCULO* or MUSCULAR) adj3 PAIN).ti,ab.	908
30	Back Pain/	2408
31	Pain Measurement/	914
32	fibromyalgia/	929
33	Chronic Pain/	7980
34	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33	18034
35	prospective studies/ or longitudinal studies/	15006
36	cohort analysis/	889
37	general practitioners/	3988
38	Retrospective Studies/	315
39	"family pract*".ti,ab.	1935
40	"general pract*".ti,ab.	8495
41	(observ* or cohort or prospectiv* or retrospectiv* or population or longitud* or community or case* control or cross* section*).ti,ab.	614867

42	35 or 36 or 37 or 38 or 39 or 40 or 41	627780
43	10 and 34 and 42	112
44	limit 43 to (human and english language)	**100**

CINAHL using NHS interface (1980 to present)

1	MORTALITY/ OR HOSPITAL MORTALITY/	15154
2	mortality.ti,ab	45926
3	CAUSE OF DEATH/	4018
4	"cause of death".ti,ab	3680
5	FATAL OUTCOME/	2216
6	fatal*.ti,ab	8192
7	DEATH/	7876
8	death.ti,ab	41030
9	dead.ti,ab	2172
10	died.ti,ab	9386
11	SURVIVAL/	13840
12	survival.ti,ab	29672
13	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12	129406
14	NECK PAIN/ OR CHRONIC PAIN/ OR BACK PAIN/ OR PAIN MEASUREMENT/	30783
15	(widespread adj3 pain).ti,ab	329
16	ARTHRALGIA/	500
17	arthralgia.ti,ab	244
18	FIBROMYALGIA/	2503
19	fibromyalgia.ti,ab	2218
20	myalgia.ti,ab	305
21	(chronic adj3 pain).ti,ab	9552
22	(joint ADJ pain).ti,ab	1301
23	(radicular ADJ pain).ti,ab	258
24	COMPLEX REGIONAL PAIN SYNDROMES/	398
25	(regional adj3 pain).ti,ab	742
26	"presence of pain".ti,ab	181
27	(mult* adj3 pain).ti,ab	1376
28	(comorbid* adj3 pain).ti,ab	176
29	"non* cancer pain".ti,ab	69
30	"non* malignant pain".ti,ab	49
31	MYOFASCIAL PAIN SYNDROMES/	717
32	(neck OR cervical adj3 pain).ti,ab	12840
33	(knee* OR hip OR hips OR shoulder* adj3 pain).ti,ab	29176

34	(foot OR feet OR ankle* OR elbow* adj3 pain).ti,ab	19010
35	(back OR lumbar OR lumbo* OR spine OR spinal adj3 pain).ti,ab	38544
36	(musculo* OR muscular adj3 pain).ti,ab	8239
37	PELVIC PAIN/	848
38	14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37	123270
39	NONEXPERIMENTAL STUDIES/ OR CASE CONTROL STUDIES/ OR PROSPECTIVE STUDIES/	149517
40	CONCURRENT PROSPECTIVE STUDIES/ OR PSEUDOLONGITUDINAL STUDIES/	55
41	RETROSPECTIVE PANEL STUDIES/ OR RETROSPECTIVE DESIGN/	55085
42	NONCONCURRENT PROSPECTIVE STUDIES/ OR CROSS SECTIONAL STUDIES/	46988
43	FAMILY PRACTICE/	8926
44	COMMUNITY HEALTH CENTERS/	2088
45	OBSERVATIONAL METHODS/	7756
46	EPIDEMIOLOGICAL RESEARCH/	17635
47	"family pract*".ti,ab	1499
48	"general pract*".ti,ab	9561
51	(observ* OR cohort OR prospectiv* OR retrospectiv* OR population OR longitud* OR community OR (case* AND control) OR (cross* AND section*)).ti,ab	336270
52	39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 51	461010
53	13 AND 38 AND 52	3263
54	53 [Limit to: (Language English)]	**3232**

Social Sciences Citation Index (SSCI)
Science Citation Index Expanded (SCI-EXPANDED)
using Web of Science (1970 to present)

# 40 (#39) AND Language=(English)	3,242
# 39 #38 AND #34 AND #11	3,388
# 38 #37 OR #36 OR #35	5,130,729
# 37 ts=(observ* OR cohort or prospectiv* OR retrospectiv* OR population OR longitud* OR community OR "case* control" OR "cross* section*")	5,066,908
# 36 ts=general pract*	101,275
# 35 ts=family pract*,ti,ab	2
# 34 #33 OR #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12	123,535
# 33 (ts= ("back pain" or "spine pain" or "spinal pain" or "lumbar pain" or	30,018

	"lumbo* pain")) AND Language=(English)	
# 32	(ts=("foot pain" or "ankle pain" or "elbow pain")) AND Language=(English)	1,183
# 31	(ts=("knee pain" or "hip pain" or "shoulder pain")) AND Language=(English)	7,143
# 30	(ts=("neck pain" or "cervical pain")) AND Language=(English)	4,716
# 29	(ts=("back pain" OR "lumbar pain" OR "lumbo* pain" OR "spine pain" OR "spinal pain")) AND Language=(English)	30,018
# 28	ts=(musculo* OR muscular near pain)	30,199
# 27	ts="pain measurement"	892
# 26	ts="myofascial pain syndromes"	134
# 25	ts="complex regional pain syndromes"	120
# 24	ts="non* malignant pain"	232
# 23	ts="non* cancer pain"	277
# 22	ts=(comorbid* near pain)	1,501
# 21	ts=(mult* near pain)	12,498
# 20	ts="presence of pain"	437
# 19	ts=(regional near pain)	3,406
# 18	ts=(radicular near pain)	1,558
# 17	ts=(joint near pain)	11,612
# 16	ts=(chronic near pain)	36,863
# 15	ts=myalgia	4,384
# 14	ts=fibromyalgia	8,943
# 13	ts=arthralgia	3,282
# 12	ts=(widespread NEAR pain)	1,613
# 11	#10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1	1,408,621
# 10	ts=survival	559,536
# 9	ts="sudden death"	17,548
# 8	ts=died	177,790
# 7	ts=dead	50,560
# 6	ts=fatal*	70,550
# 5	ts="hospital mortality"	13,410
# 4	ts="fatal outcome"	3,360
# 3	ts="cause of death"	19,405
# 2	ts=death	458,758
# 1	ts=mortality	432,078

Cochrane library: (Cochrane Database of Systematic Reviews (Cochrane Reviews), Database of Abstracts of Reviews of Effects (Other Reviews)

#1	(mortality.ti,ab)	9513
#2	mortality/	38650
#3	cause of death/	8828
#4	fatal outcome/	2323
#5	hospital mortality/	16276
#6	cause of death.ti,ab	3421
#7	fatal*.ti,ab	9513
#8	death.ti,ab	9513
#9	died.ti,ab	9513
#10	death/	24789
#11	death,sudden/	25554
#12	dead.ti,ab	9513
#13	survival/	36976
#14	survival.ti,ab	9513
#15	widespread adj3 pain.ti,ab	141
#16	arthralgia.ti,ab	9513
#17	fibromyalgia.ti,ab	9513
#18	myalgia.ti,ab	9513
#19	chronic adj3 pain.ti,ab	564
#20	joint adj pain.ti,ab	346
#21	radicular adj pain.ti,ab	31
#22	regional adj3 pain.ti,ab	218
#23	presence of pain.ti,ab	2168
#24	mult* adj3 pain.ti,ab	884
#25	musculoskeletal pain/	1887
#26	chronic pain/	8610
#27	exp joint pain/	662
#28	fibromyalgia/	930
#29	pain measurement/	17607
#30	non* cancer pain.ti,ab	1659
#31	non* malignant pain.ti,ab	524
#32	arthralgia/	997
#33	complex regional pain syndromes/	290

#34	myofascial pain syndromes/	379
#35	neck or cervical adj3 pain.ti,ab	10404
#36	knee* or hip or hips or shoulder* adj3 pain.ti,ab	15826
#37	foot or feet or ankle* or elbow* adj3 pain.ti,ab	7150
#38	back or lumbar or lumbo* or spine or spinal adj3 pain.ti,ab	16659
#39	musculo* or muscular adj3 pain.ti,ab	3443
#40	longitudinal studies/	7733
#41	cohort studies/	18545
#42	prospective studies/	96203
#43	family practice/ or general practice/	18426
#44	retrospective studies/	12135
#45	Case-Control Studies/ or Epidemiologic Methods/	8036
#46	Cross-Sectional Studies/	5307
#47	family pract*.ti,ab	9513
#48	general pract*.ti,ab	9513
#49	observ* or cohort or prospectiv* or retrospectiv* or population or longitud* or community or case* control or cross* section*.ti,ab.	267548
#50	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14)	74562
#51	(#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39)	68424
#52	(#40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49)	275080
#53	(#50 AND #51 AND #52)	13097
#54	(#53)	**5104**

Ageline using EBSCO (1978 to present)

S33	S9 and S27 and S32	77
S32	S28 or S29 or S30 or S31	51780
S31	observ* or cohort or prospectiv* or retrospectiv* or population or longitud* or community or case* control or cross* section*	51142
S30	family pract*	616
S29	general pract*	778
S28	(DE "Longitudinal Studies") OR (DE "Cohorts")	6281
S27	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or	1294

	S20 or S21 or S22 or S23 or S24 or S25 or S26	
S26	(BACK or LUMBAR or LUMBO* or SPINE or SPINAL) and PAIN	203
S25	(FOOT or FEET or ANKLE* or ELBOW*) and PAIN	63
S24	(KNEE* or HIP or HIPS or SHOULDER*) and PAIN	173
S23	(NECK or CERVICAL) and PAIN	40
S22	Myofascial pain syndrome	1
S21	(musculo* or muscular) and pain	97
S20	comorbid* and pain	119
S19	mult* and pain	506
S18	"presence of pain"	18
S17	regional and pain	22
S16	joint and pain	189
S15	chronic and pain	541
S14	Myalgia	2
S13	Fibromyalgia	20
S12	Arthralgia	1
S11	widespread and pain	20
S10	DE "Chronic Pain"	209
S9	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8	11051
S8	Survival	1486
S7	Died	1455
S6	Dead	211
S5	Death	8341
S4	fatal*	339
S3	"cause of death"	229
S2	DE "Death" OR DE "Death Causes" OR DE "Death Rates"	3519
S1	Mortality	3532

Database	No of items	Duplicates per database	Total Duplicates	Total items
Ageline	77	0	0	77
AMED	42	0	0	119
CINAHL	3232	33	33	3318
Cochrane	4775	48	81	8045
DARE	329	8	89	8366
EMBASE	4651	394	483	12623
Medline	1935	1478	1961	13080
PsychInfo	100	61	2022	13119
Web of Science	3242	1304	3326	15057
Total	18383	3326	3326	15057

Appendix II - Quality in Prognosis Studies (QUIPS)

QUality **I**n **P**rognosis **S**tudies **(QUIPS)** – Quality Appraisal Exercise

Primary Goal: Generate a list of specific issues related to potential biases in prognosis studies

Steps (for each assigned study):

- Review the methods of the assigned prognosis study
- Decide if the study methods satisfy each general statement below for the 6 biases
- Explain **WHY** you chose that rating under '*Comments'* (good or bad methods achieved)
- Provide explanation (important points or exceptions) relevant to assess studies
- Citations to methods publications are encouraged and will be extremely helpful

Study (First author, year): _____

Bias related to Study Participation	
1. The source population or population of interest is adequately described for key characteristics. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	***Comments:*** For example, what are the 'key characteristics' that need to be described for the source population?
2. The sampling frame and recruitment are adequately described, possibly including: - Methods to identify the sample (number and type used, e.g. referral patterns in healthcare settings) - Time period of recruitment - Place of recruitment (setting and geographic location) ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*

3. Inclusion and exclusion criteria are adequately described, including explicit diagnostic criteria or 'zero time' description. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
4. There is adequate participation in the study by eligible individuals. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
5. The baseline study sample (i.e. individuals entering into the study) is adequately described for key characteristics. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
6. ***Study Participation Summary:*** Is the following statement satisfied based on responses to the above questions, "The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results"? ☐ Yes ☐ Partly ☐ No ☐ Unclear	*Comments:* Which of the above questions did you consider to make this judgment?

Bias related to Study Attrition	
7. Response rate (i.e. proportion of study sample completing the study and providing outcome data) is adequate. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
8. Attempts to collect information on drop-outs are described.	*Comments:*

☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	
9. Reasons for 'loss to follow-up' are provided. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
10. Subjects lost to follow-up are adequately described for key characteristics. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
11. There are no important differences between completers and non-completers on key characteristics and outcomes. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
12. ***Study Attrition Summary:*** The following statement is satisfied based on responses to the above questions, "Loss to follow-up (from sample to study population) is not associated with key characteristics (i.e. the study data adequately represents the sample), sufficient to limit potential bias"? ☐ Yes ☐ Partly ☐ No ☐ Unclear	*Comments:*

Bias related to Prognostic Factor Measurement	
13. A clear definition or description of the prognostic factor measured is provided (e.g. including dose, level, duration of exposure, and clear specification of the method of measurement). ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
14. Continuous variables are reported or appropriate (i.e. not data dependent) cut-points are used. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
15. The prognostic factor measure and method used is adequately valid and reliable to limit misclassification bias (e.g. may include relevant outside sources of information on measurement properties, also characteristics such as blind measurement, limited reliance on recall). ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
16. Adequate proportion of sample has complete data for all relevant outcome periods. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
17. The method and setting of measurement is the same for all study participants. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
18. Appropriate methods are used if imputation is used for missing prognostic factor data.	*Comments:*

☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	
19. ***Prognostic Factor Measurement Summary:*** The following statement is satisfied based on responses to the above questions, "The prognostic factor of interest is adequately measured in study participants to sufficiently limit potential bias"? ☐ Yes ☐ Partly ☐ No ☐ Unclear	*Comments:*

Bias related to Outcome Measurement	
20. A clear definition of the outcome of interest is provided including duration of follow-up, the level and extent of the outcome construct. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
21. The outcome measure and method used is adequately valid and reliable to limit misclassification bias (e.g. may include relevant outside sources of information on measurement properties, also characteristics such as blind measurement, confirmation of outcome with valid and reliable test). ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
22. The method and setting of measurement is the same for all study participants. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*

23. ***Outcome Measurement Summary:***	*Comments:*
The following statement is satisfied based on responses to the above questions, "The outcome of interest is adequately measured in study participants to sufficiently limit potential bias"? ☐ Yes ☐ Partly ☐ No ☐ Unclear	

Bias related to Confounding Measurement and Account	
24. All important confounders, including treatments (key variables in conceptual model) are measured. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
25. Clear definitions of the important confounders measured are provided (e.g. including dose, level, and duration of exposures). ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
26. Measurement of all important confounders is adequately valid and reliable (e.g. may include relevant outside sources of information on measurement properties, also characteristics such as blind measurement, limited reliance on recall). ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
27. The method and setting of confounding measurement is the same for all study participants. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
28. Appropriate methods are used if imputation is used for missing confounder data.	*Comments:*

☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	
29. Important potential confounders are accounted for in the study design (i.e. matching for key variables, stratification, or initial assembly of comparable groups). ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
30. Important potential confounders are accounted for in the analysis (i.e. appropriate adjustment). ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
31. ***Confounding Measurement and Account Summary:*** The following statement is satisfied based on responses to the above questions, "Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest"? ☐ Yes ☐ Partly ☐ No ☐ Unclear	*Comments:*

Bias related to Analysis	
32. There is sufficient presentation of data to assess the adequacy of the analysis. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
33. The strategy for model building (i.e. inclusion of variables) is appropriate and based on a conceptual framework or model. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*

34. The selected model is adequate for the design of the study. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
35. There is no selective reporting of results. ☐ Yes ☐ Partly ☐ No ☐ Unclear ☐ Not relevant	*Comments:*
36. ***Analysis Summary:*** The following statement is satisfied based on the responses to the above questions, "The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results"? ☐ Yes ☐ Partly ☐ No ☐ Unclear	*Comments:*

Overall comments on methods in LBP prognosis studies: _____
_____
_____
_____
_____

Comments on this project: _____
_____
_____
_____

THANK YOU!

Appendix III - Missing data correlations

ELSA

```
-------------------------------------------------------------------------------
      name:  <unnamed>
       log:  S:\Data\ELSAmissing.log
  log type:  text
 opened on:  26 Jun 2015, 10:37:48

. local corrvars "Pain2 cen2 age2 sex2 education wealth phact symptomcount function smok
> e volunteerwork hehelf dep cognitiveability alc groupmem tot w4physact w4symptom w4fun
> ction w4vol w4smoke w4srhealth w4cogability w4alc w4dep w4groupmem w4casp19"

.
. foreach var of varlist Pain2 cen2 age2 sex2 education wealth phact symptomcount functi
> on smoke volunteerwork hehelf dep cognitiveability alc groupmem tot w4physact w4sympto
> m w4function w4vol w4smoke w4srhealth w4cogability w4alc w4dep w4groupmem w4casp19{
  2.
. gen m_`var' = missing(`var')
  3.
. pwcorr m_`var' `: list corrvars - var'
  4.
. }

             |  m_Pain2     cen2     age2     sex2 educat~n   wealth    phact
-------------+------------------------------------------------------------------
     m_Pain2 |   1.0000
        cen2 |  -0.0977   1.0000
        age2 |  -0.5931  -0.3038   1.0000
        sex2 |  -0.0233   0.0656   0.0013   1.0000
   education |        .   0.1479  -0.2689  -0.1542   1.0000
      wealth |        .   0.1653  -0.1523  -0.0508   0.4057   1.0000
       phact |        .   0.2767  -0.2889  -0.0687   0.2443   0.2821   1.0000
symptomcount |        .  -0.2519   0.2414   0.0453  -0.1771  -0.2402  -0.4302
```

function	.	-0.2439	0.2113	0.0546	-0.1470	-0.2166	-0.4586
smoke	.	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678	-0.0898
volunteerw~k	.	0.1177	-0.0762	0.0374	0.2576	0.2199	0.1790
hehelf	.	0.2348	-0.1705	0.0083	0.2288	0.2923	0.4010
dep	.	-0.1243	0.1089	0.1295	-0.1816	-0.2160	-0.2502
cognitivea~y	.	0.2814	-0.4438	0.0898	0.3377	0.2667	0.2555
alc	.	0.0818	-0.1267	-0.2121	0.2098	0.2320	0.1693
groupmem	.	0.0577	0.0230	0.0049	0.2824	0.2516	0.2066
tot	.	0.1849	-0.1193	0.0296	0.1667	0.2999	0.3254
w4physact	.	0.2696	-0.3264	-0.0864	0.2446	0.2815	0.4955
w4symptom	.	-0.1675	0.2411	0.0576	-0.1934	-0.2553	-0.3448
w4function	.	-0.3181	0.2918	0.0516	-0.1542	-0.1956	-0.3641
w4vol	.	0.1317	-0.1403	0.0161	0.3207	0.2604	0.1968
w4smoke	.	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907	-0.0850
w4srhealth	.	0.1637	-0.1844	-0.0163	0.2372	0.2792	0.3293
w4cogability	.	0.2381	-0.4596	0.0826	0.3437	0.2499	0.2177
w4alc	.	0.1360	-0.1656	-0.1897	0.2321	0.2593	0.1916
w4dep	.	-0.1126	0.1379	0.1317	-0.1856	-0.2248	-0.2306
w4groupmem	.	0.1253	-0.0535	0.0151	0.3304	0.3169	0.2408
w4casp19	.	0.1443	-0.1731	0.0056	0.1832	0.2683	0.2718

	sympto~t	function	smoke	volunt~k	hehelf	dep	cognit~y
symptomcount	1.0000						
function	0.6330	1.0000					
smoke	0.0605	0.0548	1.0000				
volunteerw~k	-0.1572	-0.1548	-0.1019	1.0000			
hehelf	-0.4896	-0.4521	-0.1365	0.1831	1.0000		
dep	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000	
cognitivea~y	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498	1.0000
alc	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334	0.1248
groupmem	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013	0.1113
tot	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144	0.1868
w4physact	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203	0.2583

w4symptom	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953	-0.1835
w4function	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434	-0.2572
w4vol	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174	0.2362
w4smoke	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904	-0.0144
w4srhealth	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088	0.2265
w4cogability	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462	0.5832
w4alc	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427	0.1610
w4dep	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263	0.1986
w4casp19	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			

w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_cen2	Pain2	age2	sex2	educat~n	wealth	phact
m_cen2	1.0000						
Pain2	0.0039	1.0000					
age2	-0.0402	0.0692	1.0000				
sex2	0.0021	0.0794	0.0013	1.0000			
education	.	-0.1299	-0.2689	-0.1542	1.0000		
wealth	.	-0.1706	-0.1523	-0.0508	0.4057	1.0000	
phact	.	-0.2480	-0.2889	-0.0687	0.2443	0.2821	1.0000
symptomcount	.	0.3735	0.2414	0.0453	-0.1771	-0.2402	-0.4302
function	.	0.3496	0.2113	0.0546	-0.1470	-0.2166	-0.4586
smoke	.	0.0516	-0.0585	-0.1252	-0.0932	-0.1678	-0.0898
volunteerw~k	.	-0.0818	-0.0762	0.0374	0.2576	0.2199	0.1790
hehelf	.	-0.4115	-0.1705	0.0083	0.2288	0.2923	0.4010
dep	.	0.2854	0.1089	0.1295	-0.1816	-0.2160	-0.2502
cognitivea~y	.	-0.0932	-0.4438	0.0898	0.3377	0.2667	0.2555
alc	.	-0.1295	-0.1267	-0.2121	0.2098	0.2320	0.1693
groupmem	.	-0.0801	0.0230	0.0049	0.2824	0.2516	0.2066
tot	.	-0.3145	-0.1193	0.0296	0.1667	0.2999	0.3254
w4physact	.	-0.2261	-0.3264	-0.0864	0.2446	0.2815	0.4955
w4symptom	.	0.3604	0.2411	0.0576	-0.1934	-0.2553	-0.3448
w4function	.	0.2406	0.2918	0.0516	-0.1542	-0.1956	-0.3641
w4vol	.	-0.0874	-0.1403	0.0161	0.3207	0.2604	0.1968
w4smoke	.	0.0586	-0.1209	-0.0003	-0.0991	-0.1907	-0.0850
w4srhealth	.	-0.3547	-0.1844	-0.0163	0.2372	0.2792	0.3293
w4cogability	.	-0.1047	-0.4596	0.0826	0.3437	0.2499	0.2177
w4alc	.	-0.1273	-0.1656	-0.1897	0.2321	0.2593	0.1916
w4dep	.	0.2778	0.1379	0.1317	-0.1856	-0.2248	-0.2306
w4groupmem	.	-0.1070	-0.0535	0.0151	0.3304	0.3169	0.2408
w4casp19	.	-0.2925	-0.1731	0.0056	0.1832	0.2683	0.2718

	sympto~t	function	smoke	volunt~k	hehelf	dep	cognit~y
symptomcount	1.0000						
function	0.6330	1.0000					
smoke	0.0605	0.0548	1.0000				
volunteerw~k	-0.1572	-0.1548	-0.1019	1.0000			
hehelf	-0.4896	-0.4521	-0.1365	0.1831	1.0000		
dep	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000	
cognitivea~y	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498	1.0000
alc	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334	0.1248
groupmem	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013	0.1113
tot	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144	0.1868
w4physact	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203	0.2583
w4symptom	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953	-0.1835
w4function	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434	-0.2572
w4vol	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174	0.2362
w4smoke	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904	-0.0144
w4srhealth	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088	0.2265
w4cogability	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462	0.5832
w4alc	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427	0.1610
w4dep	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263	0.1986
w4casp19	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000

w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_age2	Pain2	cen2	sex2	educat~n	wealth	phact
m_age2	.						
Pain2	.	1.0000					
cen2	.	-0.0615	1.0000				
sex2	.	0.0794	0.0656	1.0000			
education	.	-0.1299	0.1479	-0.1542	1.0000		
wealth	.	-0.1706	0.1653	-0.0508	0.4057	1.0000	
phact	.	-0.2480	0.2767	-0.0687	0.2443	0.2821	1.0000
symptomcount	.	0.3735	-0.2519	0.0453	-0.1771	-0.2402	-0.4302
function	.	0.3496	-0.2439	0.0546	-0.1470	-0.2166	-0.4586
smoke	.	0.0516	-0.0686	-0.1252	-0.0932	-0.1678	-0.0898
volunteerw~k	.	-0.0818	0.1177	0.0374	0.2576	0.2199	0.1790
hehelf	.	-0.4115	0.2348	0.0083	0.2288	0.2923	0.4010
dep	.	0.2854	-0.1243	0.1295	-0.1816	-0.2160	-0.2502
cognitivea~y	.	-0.0932	0.2814	0.0898	0.3377	0.2667	0.2555

alc	.	-0.1295	0.0818	-0.2121	0.2098	0.2320	0.1693
groupmem	.	-0.0801	0.0577	0.0049	0.2824	0.2516	0.2066
tot	.	-0.3145	0.1849	0.0296	0.1667	0.2999	0.3254
w4physact	.	-0.2261	0.2696	-0.0864	0.2446	0.2815	0.4955
w4symptom	.	0.3604	-0.1675	0.0576	-0.1934	-0.2553	-0.3448
w4function	.	0.2406	-0.3181	0.0516	-0.1542	-0.1956	-0.3641
w4vol	.	-0.0874	0.1317	0.0161	0.3207	0.2604	0.1968
w4smoke	.	0.0586	-0.0240	-0.0003	-0.0991	-0.1907	-0.0850
w4srhealth	.	-0.3547	0.1637	-0.0163	0.2372	0.2792	0.3293
w4cogability	.	-0.1047	0.2381	0.0826	0.3437	0.2499	0.2177
w4alc	.	-0.1273	0.1360	-0.1897	0.2321	0.2593	0.1916
w4dep	.	0.2778	-0.1126	0.1317	-0.1856	-0.2248	-0.2306
w4groupmem	.	-0.1070	0.1253	0.0151	0.3304	0.3169	0.2408
w4casp19	.	-0.2925	0.1443	0.0056	0.1832	0.2683	0.2718

	sympto~t	function	smoke	volunt~k	hehelf	dep	cognit~y
symptomcount	1.0000						
function	0.6330	1.0000					
smoke	0.0605	0.0548	1.0000				
volunteerw~k	-0.1572	-0.1548	-0.1019	1.0000			
hehelf	-0.4896	-0.4521	-0.1365	0.1831	1.0000		
dep	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000	
cognitivea~y	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498	1.0000
alc	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334	0.1248
groupmem	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013	0.1113
tot	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144	0.1868
w4physact	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203	0.2583
w4symptom	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953	-0.1835
w4function	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434	-0.2572
w4vol	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174	0.2362
w4smoke	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904	-0.0144
w4srhealth	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088	0.2265
w4cogability	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462	0.5832

w4alc	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427	0.1610
w4dep	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263	0.1986
w4casp19	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_sex2	Pain2	cen2	age2	educat~n	wealth	phact

m_sex2	.						
Pain2	.	1.0000					
cen2	.	-0.0615	1.0000				
age2	.	0.0692	-0.3038	1.0000			
education	.	-0.1299	0.1479	-0.2689	1.0000		
wealth	.	-0.1706	0.1653	-0.1523	0.4057	1.0000	
phact	.	-0.2480	0.2767	-0.2889	0.2443	0.2821	1.0000
symptomcount	.	0.3735	-0.2519	0.2414	-0.1771	-0.2402	-0.4302
function	.	0.3496	-0.2439	0.2113	-0.1470	-0.2166	-0.4586
smoke	.	0.0516	-0.0686	-0.0585	-0.0932	-0.1678	-0.0898
volunteerw~k	.	-0.0818	0.1177	-0.0762	0.2576	0.2199	0.1790
hehelf	.	-0.4115	0.2348	-0.1705	0.2288	0.2923	0.4010
dep	.	0.2854	-0.1243	0.1089	-0.1816	-0.2160	-0.2502
cognitivea~y	.	-0.0932	0.2814	-0.4438	0.3377	0.2667	0.2555
alc	.	-0.1295	0.0818	-0.1267	0.2098	0.2320	0.1693
groupmem	.	-0.0801	0.0577	0.0230	0.2824	0.2516	0.2066
tot	.	-0.3145	0.1849	-0.1193	0.1667	0.2999	0.3254
w4physact	.	-0.2261	0.2696	-0.3264	0.2446	0.2815	0.4955
w4symptom	.	0.3604	-0.1675	0.2411	-0.1934	-0.2553	-0.3448
w4function	.	0.2406	-0.3181	0.2918	-0.1542	-0.1956	-0.3641
w4vol	.	-0.0874	0.1317	-0.1403	0.3207	0.2604	0.1968
w4smoke	.	0.0586	-0.0240	-0.1209	-0.0991	-0.1907	-0.0850
w4srhealth	.	-0.3547	0.1637	-0.1844	0.2372	0.2792	0.3293
w4cogability	.	-0.1047	0.2381	-0.4596	0.3437	0.2499	0.2177
w4alc	.	-0.1273	0.1360	-0.1656	0.2321	0.2593	0.1916
w4dep	.	0.2778	-0.1126	0.1379	-0.1856	-0.2248	-0.2306
w4groupmem	.	-0.1070	0.1253	-0.0535	0.3304	0.3169	0.2408
w4casp19	.	-0.2925	0.1443	-0.1731	0.1832	0.2683	0.2718

	sympto~t	function	smoke	volunt~k	hehelf	dep	cognit~y
symptomcount	1.0000						
function	0.6330	1.0000					
smoke	0.0605	0.0548	1.0000				

volunteerw~k	-0.1572	-0.1548	-0.1019	1.0000			
hehelf	-0.4896	-0.4521	-0.1365	0.1831	1.0000		
dep	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000	
cognitivea~y	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498	1.0000
alc	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334	0.1248
groupmem	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013	0.1113
tot	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144	0.1868
w4physact	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203	0.2583
w4symptom	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953	-0.1835
w4function	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434	-0.2572
w4vol	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174	0.2362
w4smoke	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904	-0.0144
w4srhealth	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088	0.2265
w4cogability	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462	0.5832
w4alc	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427	0.1610
w4dep	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263	0.1986
w4casp19	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572

w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_educ~n	Pain2	cen2	age2	sex2	wealth	phact
m_education	1.0000						
Pain2	-0.0072	1.0000					
cen2	-0.0015	-0.0615	1.0000				
age2	-0.3721	0.0692	-0.3038	1.0000			
sex2	0.0488	0.0794	0.0656	0.0013	1.0000		
wealth	-0.0001	-0.1706	0.1653	-0.1523	-0.0508	1.0000	
phact	0.0078	-0.2480	0.2767	-0.2889	-0.0687	0.2821	1.0000
symptomcount	-0.0050	0.3735	-0.2519	0.2414	0.0453	-0.2402	-0.4302
function	0.0028	0.3496	-0.2439	0.2113	0.0546	-0.2166	-0.4586
smoke	-0.0156	0.0516	-0.0686	-0.0585	-0.1252	-0.1678	-0.0898
volunteerw~k	0.0124	-0.0818	0.1177	-0.0762	0.0374	0.2199	0.1790
hehelf	0.0056	-0.4115	0.2348	-0.1705	0.0083	0.2923	0.4010
dep	-0.0052	0.2854	-0.1243	0.1089	0.1295	-0.2160	-0.2502
cognitivea~y	-0.0084	-0.0932	0.2814	-0.4438	0.0898	0.2667	0.2555
alc	0.0111	-0.1295	0.0818	-0.1267	-0.2121	0.2320	0.1693
groupmem	-0.0160	-0.0801	0.0577	0.0230	0.0049	0.2516	0.2066
tot	0.0007	-0.3145	0.1849	-0.1193	0.0296	0.2999	0.3254
w4physact	-0.0019	-0.2261	0.2696	-0.3264	-0.0864	0.2815	0.4955
w4symptom	-0.0094	0.3604	-0.1675	0.2411	0.0576	-0.2553	-0.3448
w4function	0.0125	0.2406	-0.3181	0.2918	0.0516	-0.1956	-0.3641

w4vol	0.0106	-0.0874	0.1317	-0.1403	0.0161	0.2604	0.1968
w4smoke	0.0136	0.0586	-0.0240	-0.1209	-0.0003	-0.1907	-0.0850
w4srhealth	-0.0061	-0.3547	0.1637	-0.1844	-0.0163	0.2792	0.3293
w4cogability	-0.0152	-0.1047	0.2381	-0.4596	0.0826	0.2499	0.2177
w4alc	-0.0023	-0.1273	0.1360	-0.1656	-0.1897	0.2593	0.1916
w4dep	-0.0051	0.2778	-0.1126	0.1379	0.1317	-0.2248	-0.2306
w4groupmem	0.0045	-0.1070	0.1253	-0.0535	0.0151	0.3169	0.2408
w4casp19	-0.0130	-0.2925	0.1443	-0.1731	0.0056	0.2683	0.2718

	sympto~t	function	smoke	volunt~k	hehelf	dep	cognit~y
symptomcount	1.0000						
function	0.6330	1.0000					
smoke	0.0605	0.0548	1.0000				
volunteerw~k	-0.1572	-0.1548	-0.1019	1.0000			
hehelf	-0.4896	-0.4521	-0.1365	0.1831	1.0000		
dep	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000	
cognitivea~y	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498	1.0000
alc	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334	0.1248
groupmem	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013	0.1113
tot	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144	0.1868
w4physact	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203	0.2583
w4symptom	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953	-0.1835
w4function	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434	-0.2572
w4vol	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174	0.2362
w4smoke	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904	-0.0144
w4srhealth	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088	0.2265
w4cogability	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462	0.5832
w4alc	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427	0.1610
w4dep	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263	0.1986
w4casp19	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol

alc	1.0000							
groupmem	0.1321	1.0000						
tot	0.1640	0.1924	1.0000					
w4physact	0.1807	0.1749	0.2924	1.0000				
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000			
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000		
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000	
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131	
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104	
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455	
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459	
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389	
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572	
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796	

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_wealth	Pain2	cen2	age2	sex2	educat~n	phact
m_wealth	1.0000						
Pain2	-0.0114	1.0000					
cen2	0.0165	-0.0615	1.0000				
age2	-0.3578	0.0692	-0.3038	1.0000			
sex2	0.0516	0.0794	0.0656	0.0013	1.0000		
education	0.0336	-0.1299	0.1479	-0.2689	-0.1542	1.0000	

phact	0.0244	-0.2480	0.2767	-0.2889	-0.0687	0.2443	1.0000
symptomcount	-0.0248	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.4302
function	-0.0274	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.4586
smoke	-0.0018	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.0898
volunteerw~k	-0.0042	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.1790
hehelf	0.0140	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.4010
dep	-0.0229	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2502
cognitivea~y	0.0411	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2555
alc	0.0167	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.1693
groupmem	0.0194	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2066
tot	0.0121	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.3254
w4physact	0.0171	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.4955
w4symptom	-0.0179	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.3448
w4function	-0.0294	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.3641
w4vol	0.0187	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.1968
w4smoke	-0.0067	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.0850
w4srhealth	0.0187	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.3293
w4cogability	0.0364	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2177
w4alc	0.0031	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.1916
w4dep	-0.0339	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2306
w4groupmem	0.0060	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.2408
w4casp19	0.0185	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2718

	sympto~t	function	smoke	volunt~k	hehelf	dep	cognit~y
symptomcount	1.0000						
function	0.6330	1.0000					
smoke	0.0605	0.0548	1.0000				
volunteerw~k	-0.1572	-0.1548	-0.1019	1.0000			
hehelf	-0.4896	-0.4521	-0.1365	0.1831	1.0000		
dep	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000	
cognitivea~y	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498	1.0000
alc	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334	0.1248
groupmem	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013	0.1113

tot	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144	0.1868
w4physact	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203	0.2583
w4symptom	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953	-0.1835
w4function	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434	-0.2572
w4vol	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174	0.2362
w4smoke	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904	-0.0144
w4srhealth	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088	0.2265
w4cogability	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462	0.5832
w4alc	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427	0.1610
w4dep	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263	0.1986
w4casp19	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					

w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_phact	Pain2	cen2	age2	sex2	educat~n	wealth
m_phact	1.0000						
Pain2	-0.0091	1.0000					
cen2	-0.0044	-0.0615	1.0000				
age2	-0.3759	0.0692	-0.3038	1.0000			
sex2	0.0532	0.0794	0.0656	0.0013	1.0000		
education	.	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	.	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
symptomcount	.	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	.	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	.	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	.	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	.	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	.	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	.	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	.	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	.	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	.	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	.	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	.	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	.	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	.	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	.	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	.	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	.	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	.	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	.	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248

w4groupmem	.	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	.	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	sympto~t	function	smoke	volunt~k	hehelf	dep	cognit~y
symptomcount	1.0000						
function	0.6330	1.0000					
smoke	0.0605	0.0548	1.0000				
volunteerw~k	-0.1572	-0.1548	-0.1019	1.0000			
hehelf	-0.4896	-0.4521	-0.1365	0.1831	1.0000		
dep	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000	
cognitivea~y	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498	1.0000
alc	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334	0.1248
groupmem	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013	0.1113
tot	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144	0.1868
w4physact	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203	0.2583
w4symptom	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953	-0.1835
w4function	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434	-0.2572
w4vol	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174	0.2362
w4smoke	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904	-0.0144
w4srhealth	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088	0.2265
w4cogability	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462	0.5832
w4alc	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427	0.1610
w4dep	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263	0.1986
w4casp19	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		

w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_symp~t	Pain2	cen2	age2	sex2	educat~n	wealth
m_symptomc~t	1.0000						
Pain2	-0.0091	1.0000					
cen2	-0.0044	-0.0615	1.0000				
age2	-0.3759	0.0692	-0.3038	1.0000			
sex2	0.0532	0.0794	0.0656	0.0013	1.0000		
education	.	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	.	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	.	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
function	.	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	.	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	.	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	.	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923

dep	.	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	.	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	.	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	.	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	.	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	.	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	.	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	.	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	.	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	.	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	.	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	.	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	.	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	.	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	.	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	.	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	function	smoke	volunt~k	hehelf	dep	cognit~y
phact	1.0000						
function	-0.4586	1.0000					
smoke	-0.0898	0.0548	1.0000				
volunteerw~k	0.1790	-0.1548	-0.1019	1.0000			
hehelf	0.4010	-0.4521	-0.1365	0.1831	1.0000		
dep	-0.2502	0.3358	0.0705	-0.1114	-0.3694	1.0000	
cognitivea~y	0.2555	-0.2124	-0.0399	0.1667	0.2406	-0.1498	1.0000
alc	0.1693	-0.1609	0.0332	0.0578	0.1800	-0.1334	0.1248
groupmem	0.2066	-0.1213	-0.1321	0.3689	0.1653	-0.1013	0.1113
tot	0.3254	-0.4205	-0.1107	0.1556	0.4946	-0.4144	0.1868
w4physact	0.4955	-0.3713	-0.1037	0.1568	0.3641	-0.2203	0.2583
w4symptom	-0.3448	0.4665	0.1035	-0.1259	-0.4425	0.2953	-0.1835
w4function	-0.3641	0.6061	0.0457	-0.1312	-0.3676	0.2434	-0.2572
w4vol	0.1968	-0.1557	-0.1270	0.4751	0.1804	-0.1174	0.2362
w4smoke	-0.0850	0.0701	0.6205	-0.0939	-0.1259	0.0904	-0.0144

w4srhealth	0.3293	-0.3770	-0.1459	0.1316	0.6283	-0.3088	0.2265
w4cogability	0.2177	-0.1807	-0.0621	0.1604	0.2079	-0.1462	0.5832
w4alc	0.1916	-0.1814	0.0024	0.0811	0.1990	-0.1427	0.1610
w4dep	-0.2306	0.3136	0.0792	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	0.2408	-0.1481	-0.1700	0.3838	0.2160	-0.1263	0.1986
w4casp19	0.2718	-0.3317	-0.1100	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_func~n	Pain2	cen2	age2	sex2	educat~n	wealth
m_function	1.0000						
Pain2	-0.0095	1.0000					
cen2	-0.0057	-0.0615	1.0000				
age2	-0.3750	0.0692	-0.3038	1.0000			
sex2	0.0535	0.0794	0.0656	0.0013	1.0000		
education	-0.0110	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	0.0152	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.0239	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.0159	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
smoke	0.0033	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.0065	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.0208	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	-0.0011	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	0.0002	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0143	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	.	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0165	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.0260	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.0423	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.0305	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.0101	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	-0.0047	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.0136	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.0212	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.0134	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0192	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	.	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0115	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	smoke	volunt~k	hehelf	dep	cognit~y
phact	1.0000						

symptomcount	-0.4302	1.0000					
smoke	-0.0898	0.0605	1.0000				
volunteerw~k	0.1790	-0.1572	-0.1019	1.0000			
hehelf	0.4010	-0.4896	-0.1365	0.1831	1.0000		
dep	-0.2502	0.3456	0.0705	-0.1114	-0.3694	1.0000	
cognitivea~y	0.2555	-0.2164	-0.0399	0.1667	0.2406	-0.1498	1.0000
alc	0.1693	-0.1749	0.0332	0.0578	0.1800	-0.1334	0.1248
groupmem	0.2066	-0.1269	-0.1321	0.3689	0.1653	-0.1013	0.1113
tot	0.3254	-0.4203	-0.1107	0.1556	0.4946	-0.4144	0.1868
w4physact	0.4955	-0.3741	-0.1037	0.1568	0.3641	-0.2203	0.2583
w4symptom	-0.3448	0.5781	0.1035	-0.1259	-0.4425	0.2953	-0.1835
w4function	-0.3641	0.4616	0.0457	-0.1312	-0.3676	0.2434	-0.2572
w4vol	0.1968	-0.1532	-0.1270	0.4751	0.1804	-0.1174	0.2362
w4smoke	-0.0850	0.0820	0.6205	-0.0939	-0.1259	0.0904	-0.0144
w4srhealth	0.3293	-0.4043	-0.1459	0.1316	0.6283	-0.3088	0.2265
w4cogability	0.2177	-0.2020	-0.0621	0.1604	0.2079	-0.1462	0.5832
w4alc	0.1916	-0.1981	0.0024	0.0811	0.1990	-0.1427	0.1610
w4dep	-0.2306	0.3054	0.0792	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	0.2408	-0.1603	-0.1700	0.3838	0.2160	-0.1263	0.1986
w4casp19	0.2718	-0.3465	-0.1100	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459

w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_smoke	Pain2	cen2	age2	sex2	educat~n	wealth
m_smoke	1.0000						
Pain2	-0.0092	1.0000					
cen2	-0.0036	-0.0615	1.0000				
age2	-0.3754	0.0692	-0.3038	1.0000			
sex2	0.0533	0.0794	0.0656	0.0013	1.0000		
education	0.0058	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	0.0162	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	0.0010	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	-0.0089	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	-0.0085	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
volunteerw~k	0.0026	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	0.0137	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	-0.0019	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.0014	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	0.0129	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	0.0048	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0085	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	0.0104	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815

w4symptom	-0.0114	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	-0.0099	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.0026	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	-0.0081	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	0.0038	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	0.0194	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	0.0211	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	-0.0108	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	0.0113	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	0.0053	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	volunt~k	hehelf	dep	cognit~y
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
volunteerw~k	0.1790	-0.1572	-0.1548	1.0000			
hehelf	0.4010	-0.4896	-0.4521	0.1831	1.0000		
dep	-0.2502	0.3456	0.3358	-0.1114	-0.3694	1.0000	
cognitivea~y	0.2555	-0.2164	-0.2124	0.1667	0.2406	-0.1498	1.0000
alc	0.1693	-0.1749	-0.1609	0.0578	0.1800	-0.1334	0.1248
groupmem	0.2066	-0.1269	-0.1213	0.3689	0.1653	-0.1013	0.1113
tot	0.3254	-0.4203	-0.4205	0.1556	0.4946	-0.4144	0.1868
w4physact	0.4955	-0.3741	-0.3713	0.1568	0.3641	-0.2203	0.2583
w4symptom	-0.3448	0.5781	0.4665	-0.1259	-0.4425	0.2953	-0.1835
w4function	-0.3641	0.4616	0.6061	-0.1312	-0.3676	0.2434	-0.2572
w4vol	0.1968	-0.1532	-0.1557	0.4751	0.1804	-0.1174	0.2362
w4smoke	-0.0850	0.0820	0.0701	-0.0939	-0.1259	0.0904	-0.0144
w4srhealth	0.3293	-0.4043	-0.3770	0.1316	0.6283	-0.3088	0.2265
w4cogability	0.2177	-0.2020	-0.1807	0.1604	0.2079	-0.1462	0.5832
w4alc	0.1916	-0.1981	-0.1814	0.0811	0.1990	-0.1427	0.1610
w4dep	-0.2306	0.3054	0.3136	-0.0928	-0.3247	0.4339	-0.1584
w4groupmem	0.2408	-0.1603	-0.1481	0.3838	0.2160	-0.1263	0.1986
w4casp19	0.2718	-0.3465	-0.3317	0.1247	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_volu~k	Pain2	cen2	age2	sex2	educat~n	wealth
m_voluntee~k	1.0000						
Pain2	-0.0089	1.0000					
cen2	-0.0039	-0.0615	1.0000				
age2	-0.3755	0.0692	-0.3038	1.0000			

sex2	0.0530	0.0794	0.0656	0.0013	1.0000		
education	0.0014	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	0.0108	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	0.0008	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	-0.0072	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	-0.0069	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	-0.0173	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
hehelf	-0.0091	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	-0.0124	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	0.0108	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	0.0129	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	0.0048	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	0.0043	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	0.0014	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	-0.0066	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	-0.0057	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	0.0157	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	-0.0047	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.0018	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	0.0066	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	0.0122	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	-0.0094	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	0.0065	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	0.0112	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	hehelf	dep	cognit~y
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
hehelf	0.4010	-0.4896	-0.4521	-0.1365	1.0000		
dep	-0.2502	0.3456	0.3358	0.0705	-0.3694	1.0000	
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.2406	-0.1498	1.0000

alc	0.1693	-0.1749	-0.1609	0.0332	0.1800	-0.1334	0.1248
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.1653	-0.1013	0.1113
tot	0.3254	-0.4203	-0.4205	-0.1107	0.4946	-0.4144	0.1868
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.3641	-0.2203	0.2583
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.4425	0.2953	-0.1835
w4function	-0.3641	0.4616	0.6061	0.0457	-0.3676	0.2434	-0.2572
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.1804	-0.1174	0.2362
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.1259	0.0904	-0.0144
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.6283	-0.3088	0.2265
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.2079	-0.1462	0.5832
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.1990	-0.1427	0.1610
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.3247	0.4339	-0.1584
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.2160	-0.1263	0.1986
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.4354	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19

w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_hehelf	Pain2	cen2	age2	sex2	educat~n	wealth
m_hehelf	1.0000						
Pain2	-0.0081	1.0000					
cen2	-0.0062	-0.0615	1.0000				
age2	-0.3740	0.0692	-0.3038	1.0000			
sex2	0.0516	0.0794	0.0656	0.0013	1.0000		
education	0.0032	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.0205	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.0207	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.0262	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.0024	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	-0.0065	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.0038	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
dep	-0.0059	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.0143	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0052	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0129	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0343	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.0054	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.0121	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.0041	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.0175	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	-0.0081	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.0303	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.0166	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499

w4alc	-0.0084	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0167	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.0210	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0186	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	dep	cognit~y
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	1.0000	
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	-0.1498	1.0000
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	-0.1334	0.1248
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	-0.1013	0.1113
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	-0.4144	0.1868
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	-0.2203	0.2583
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	0.2953	-0.1835
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	0.2434	-0.2572
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	-0.1174	0.2362
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	0.0904	-0.0144
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	-0.3088	0.2265
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	-0.1462	0.5832
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	-0.1427	0.1610
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	0.4339	-0.1584
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	-0.1263	0.1986
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	-0.3439	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				

w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_dep	Pain2	cen2	age2	sex2	educat~n	wealth
m_dep	1.0000						
Pain2	-0.0066	1.0000					
cen2	-0.0141	-0.0615	1.0000				
age2	-0.3660	0.0692	-0.3038	1.0000			
sex2	0.0466	0.0794	0.0656	0.0013	1.0000		
education	-0.0140	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.0147	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.0444	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.0254	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.0723	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166

smoke	-0.0111	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.0049	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.0302	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
cognitivea~y	-0.0421	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	0.0223	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	0.0082	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	0.0006	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.0324	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	-0.0020	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.0191	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.0142	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	0.0023	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	0.0005	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.0039	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.0161	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0045	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.0109	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	0.0037	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	cognit~y
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	1.0000
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	0.1248
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	0.1113
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	0.1868
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	0.2583
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	-0.1835
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	-0.2572

w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	0.2362
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	-0.0144
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	0.2265
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	0.5832
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	0.1610
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	-0.1584
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	0.1986
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	0.1802

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	

w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_cogn~y	Pain2	cen2	age2	sex2	educat~n	wealth
m_cognitiv~y	1.0000						
Pain2	0.0002	1.0000					
cen2	-0.0233	-0.0615	1.0000				
age2	-0.3558	0.0692	-0.3038	1.0000			
sex2	0.0429	0.0794	0.0656	0.0013	1.0000		
education	-0.0024	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.0074	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.0554	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.0321	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.0787	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	-0.0071	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.0224	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.0368	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	-0.0751	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
alc	0.0051	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0183	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0239	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.0518	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	-0.0058	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.0191	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.0124	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	0.0051	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.0103	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.0396	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.0199	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0103	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.0293	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	0.0005	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep

phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
alc	1.0000						
groupmem	0.1321	1.0000					
tot	0.1640	0.1924	1.0000				
w4physact	0.1807	0.1749	0.2924	1.0000			
w4symptom	-0.1758	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104

w4cogability	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_alc	Pain2	cen2	age2	sex2	educat~n	wealth
m_alc	1.0000						
Pain2	0.0155	1.0000					
cen2	-0.1327	-0.0615	1.0000				
age2	-0.1389	0.0692	-0.3038	1.0000			
sex2	0.0332	0.0794	0.0656	0.0013	1.0000		
education	-0.1161	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1488	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1453	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1098	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1445	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0383	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.0939	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1246	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0919	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.2158	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
groupmem	-0.0103	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516

tot	-0.0224	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.1482	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.0710	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.1552	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.1054	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	0.0591	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.1060	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.1486	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.1506	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0825	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.1488	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0723	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339

w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	groupmem	tot	w4phys~t	w4symp~m	w4func~n	w4vol
cognitivea~y	1.0000						
groupmem	0.1113	1.0000					
tot	0.1868	0.1924	1.0000				
w4physact	0.2583	0.1749	0.2924	1.0000			
w4symptom	-0.1835	-0.1076	-0.3523	-0.4082	1.0000		
w4function	-0.2572	-0.0850	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.2362	0.3600	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0144	-0.1439	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.2265	0.1400	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.5832	0.1198	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.1610	0.1198	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1584	-0.0975	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1986	0.5966	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1802	0.1558	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_grou~m	Pain2	cen2	age2	sex2	educat~n	wealth
m_groupmem	1.0000						
Pain2	0.0360	1.0000					

cen2	-0.1228	-0.0615	1.0000				
age2	-0.1071	0.0692	-0.3038	1.0000			
sex2	0.0410	0.0794	0.0656	0.0013	1.0000		
education	-0.1648	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1762	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1556	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1341	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1528	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0465	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1337	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1418	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.1170	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.2122	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0769	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
tot	-0.0651	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.1637	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.0898	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.1427	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.1487	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	0.0740	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.1196	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.1562	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.1421	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0985	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.1836	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0805	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		

hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	tot	w4phys~t	w4symp~m	w4func~n	w4vol
cognitivea~y	1.0000						
alc	0.1248	1.0000					
tot	0.1868	0.1640	1.0000				
w4physact	0.2583	0.1807	0.2924	1.0000			
w4symptom	-0.1835	-0.1758	-0.3523	-0.4082	1.0000		
w4function	-0.2572	-0.1572	-0.3393	-0.4680	0.4652	1.0000	
w4vol	0.2362	0.0961	0.1745	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0144	-0.0651	-0.1311	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.2265	0.1763	0.4413	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.5832	0.1205	0.1618	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.1610	0.6525	0.1660	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1584	-0.1353	-0.3725	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1986	0.1384	0.2120	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1802	0.1590	0.7096	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_tot	Pain2	cen2	age2	sex2	educat~n	wealth
m_tot	1.0000						
Pain2	0.0458	1.0000					
cen2	-0.1635	-0.0615	1.0000				
age2	-0.0333	0.0692	-0.3038	1.0000			
sex2	0.0493	0.0794	0.0656	0.0013	1.0000		
education	-0.1964	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1911	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1977	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1614	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1795	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0267	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1274	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1715	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.1458	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.2644	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0928	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0633	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
w4physact	-0.1890	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.1143	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.1713	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.1365	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	0.0372	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907

w4srhealth	-0.1494	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.2044	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.1658	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.1267	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.1604	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0987	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	groupmem	w4phys~t	w4symp~m	w4func~n	w4vol
cognitivea~y	1.0000						

alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
w4physact	0.2583	0.1807	0.1749	1.0000			
w4symptom	-0.1835	-0.1758	-0.1076	-0.4082	1.0000		
w4function	-0.2572	-0.1572	-0.0850	-0.4680	0.4652	1.0000	
w4vol	0.2362	0.0961	0.3600	0.2554	-0.1635	-0.1903	1.0000
w4smoke	-0.0144	-0.0651	-0.1439	-0.1032	0.0859	0.0307	-0.1131
w4srhealth	0.2265	0.1763	0.1400	0.4106	-0.5202	-0.4396	0.2104
w4cogability	0.5832	0.1205	0.1198	0.2829	-0.2429	-0.2520	0.2455
w4alc	0.1610	0.6525	0.1198	0.2581	-0.1895	-0.2446	0.1459
w4dep	-0.1584	-0.1353	-0.0975	-0.2827	0.3858	0.3388	-0.1389
w4groupmem	0.1986	0.1384	0.5966	0.2814	-0.1526	-0.1867	0.4572
w4casp19	0.1802	0.1590	0.1558	0.3211	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_w4ph~t	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4physact	1.0000						
Pain2	0.0454	1.0000					
cen2	-0.3317	-0.0615	1.0000				
age2	-0.0516	0.0692	-0.3038	1.0000			
sex2	-0.0050	0.0794	0.0656	0.0013	1.0000		
education	-0.1308	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1265	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1673	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821

symptomcount	0.1390	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1210	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0528	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1142	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1494	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0624	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.1791	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0391	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0830	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0884	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4symptom	.	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	.	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	.	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	.	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	.	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	.	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	.	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	.	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	.	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	.	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144

w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	groupmem	tot	w4symp~m	w4func~n	w4vol
cognitivea~y	1.0000						
alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
tot	0.1868	0.1640	0.1924	1.0000			
w4symptom	-0.1835	-0.1758	-0.1076	-0.3523	1.0000		
w4function	-0.2572	-0.1572	-0.0850	-0.3393	0.4652	1.0000	
w4vol	0.2362	0.0961	0.3600	0.1745	-0.1635	-0.1903	1.0000
w4smoke	-0.0144	-0.0651	-0.1439	-0.1311	0.0859	0.0307	-0.1131
w4srhealth	0.2265	0.1763	0.1400	0.4413	-0.5202	-0.4396	0.2104
w4cogability	0.5832	0.1205	0.1198	0.1618	-0.2429	-0.2520	0.2455
w4alc	0.1610	0.6525	0.1198	0.1660	-0.1895	-0.2446	0.1459
w4dep	-0.1584	-0.1353	-0.0975	-0.3725	0.3858	0.3388	-0.1389
w4groupmem	0.1986	0.1384	0.5966	0.2120	-0.1526	-0.1867	0.4572
w4casp19	0.1802	0.1590	0.1558	0.7096	-0.4019	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			

w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_w4sy~m	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4symptom	1.0000						
Pain2	0.0454	1.0000					
cen2	-0.3317	-0.0615	1.0000				
age2	-0.0516	0.0692	-0.3038	1.0000			
sex2	-0.0050	0.0794	0.0656	0.0013	1.0000		
education	-0.1308	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1265	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1673	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1390	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1210	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0528	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1142	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1494	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0624	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.1791	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0391	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0830	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0884	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	.	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4function	.	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	.	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	.	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	.	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	.	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	.	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	.	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	.	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	.	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	groupmem	tot	w4phys~t	w4func~n	w4vol
cognitivea~y	1.0000						
alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
tot	0.1868	0.1640	0.1924	1.0000			
w4physact	0.2583	0.1807	0.1749	0.2924	1.0000		
w4function	-0.2572	-0.1572	-0.0850	-0.3393	-0.4680	1.0000	
w4vol	0.2362	0.0961	0.3600	0.1745	0.2554	-0.1903	1.0000

w4smoke	-0.0144	-0.0651	-0.1439	-0.1311	-0.1032	0.0307	-0.1131
w4srhealth	0.2265	0.1763	0.1400	0.4413	0.4106	-0.4396	0.2104
w4cogability	0.5832	0.1205	0.1198	0.1618	0.2829	-0.2520	0.2455
w4alc	0.1610	0.6525	0.1198	0.1660	0.2581	-0.2446	0.1459
w4dep	-0.1584	-0.1353	-0.0975	-0.3725	-0.2827	0.3388	-0.1389
w4groupmem	0.1986	0.1384	0.5966	0.2120	0.2814	-0.1867	0.4572
w4casp19	0.1802	0.1590	0.1558	0.7096	0.3211	-0.3917	0.1796

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_w4fu~n	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4function	1.0000						
Pain2	0.0454	1.0000					
cen2	-0.3317	-0.0615	1.0000				
age2	-0.0516	0.0692	-0.3038	1.0000			
sex2	-0.0050	0.0794	0.0656	0.0013	1.0000		
education	-0.1308	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1265	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1673	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1390	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1210	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0528	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1142	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1494	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0624	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160

cognitivea~y	-0.1791	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0391	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0830	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0884	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	.	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	.	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4vol	.	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	.	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	.	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	.	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	.	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	.	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	.	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	.	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462

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       w4alc |   0.1916  -0.1981  -0.1814   0.0024   0.0811   0.1990  -0.1427
       w4dep |  -0.2306   0.3054   0.3136   0.0792  -0.0928  -0.3247   0.4339
  w4groupmem |   0.2408  -0.1603  -0.1481  -0.1700   0.3838   0.2160  -0.1263
    w4casp19 |   0.2718  -0.3465  -0.3317  -0.1100   0.1247   0.4354  -0.3439

             | cognit~y      alc groupmem      tot w4phys~t w4symp~m    w4vol
-------------+------------------------------------------------------------------
cognitivea~y |   1.0000
         alc |   0.1248   1.0000
    groupmem |   0.1113   0.1321   1.0000
         tot |   0.1868   0.1640   0.1924   1.0000
   w4physact |   0.2583   0.1807   0.1749   0.2924   1.0000
   w4symptom |  -0.1835  -0.1758  -0.1076  -0.3523  -0.4082   1.0000
       w4vol |   0.2362   0.0961   0.3600   0.1745   0.2554  -0.1635   1.0000
     w4smoke |  -0.0144  -0.0651  -0.1439  -0.1311  -0.1032   0.0859  -0.1131
  w4srhealth |   0.2265   0.1763   0.1400   0.4413   0.4106  -0.5202   0.2104
w4cogability |   0.5832   0.1205   0.1198   0.1618   0.2829  -0.2429   0.2455
       w4alc |   0.1610   0.6525   0.1198   0.1660   0.2581  -0.1895   0.1459
       w4dep |  -0.1584  -0.1353  -0.0975  -0.3725  -0.2827   0.3858  -0.1389
  w4groupmem |   0.1986   0.1384   0.5966   0.2120   0.2814  -0.1526   0.4572
    w4casp19 |   0.1802   0.1590   0.1558   0.7096   0.3211  -0.4019   0.1796

             |  w4smoke w4srhe~h w4coga~y    w4alc    w4dep w4grou~m w4casp19
-------------+------------------------------------------------------------------
     w4smoke |   1.0000
  w4srhealth |  -0.1211   1.0000
w4cogability |  -0.0345   0.2585   1.0000
       w4alc |  -0.0792   0.2169   0.1786   1.0000
       w4dep |   0.0800  -0.4030  -0.1927  -0.1755   1.0000
  w4groupmem |  -0.1745   0.2151   0.2155   0.2824  -0.1467   1.0000
    w4casp19 |  -0.1122   0.5114   0.2105   0.1696  -0.4561   0.2110   1.0000

             |  m_w4vol    Pain2     cen2     age2     sex2 educat~n   wealth
-------------+------------------------------------------------------------------
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m_w4vol	1.0000						
Pain2	0.0448	1.0000					
cen2	-0.3340	-0.0615	1.0000				
age2	-0.0490	0.0692	-0.3038	1.0000			
sex2	-0.0054	0.0794	0.0656	0.0013	1.0000		
education	-0.1319	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1287	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1698	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1397	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1219	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0513	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1155	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1507	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0608	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.1827	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0399	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0841	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0890	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.0533	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.0446	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.0767	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4smoke	-0.0115	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.0416	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.0746	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.0427	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	.	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.0501	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0012	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				

smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n
cognitivea~y	1.0000						
alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
tot	0.1868	0.1640	0.1924	1.0000			
w4physact	0.2583	0.1807	0.1749	0.2924	1.0000		
w4symptom	-0.1835	-0.1758	-0.1076	-0.3523	-0.4082	1.0000	
w4function	-0.2572	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000
w4smoke	-0.0144	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307
w4srhealth	0.2265	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396
w4cogability	0.5832	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520
w4alc	0.1610	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446
w4dep	-0.1584	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388
w4groupmem	0.1986	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867

w4casp19	0.1802	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917

	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4smoke	1.0000						
w4srhealth	-0.1211	1.0000					
w4cogability	-0.0345	0.2585	1.0000				
w4alc	-0.0792	0.2169	0.1786	1.0000			
w4dep	0.0800	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	-0.1745	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	-0.1122	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_w4sm~e	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4smoke	1.0000						
Pain2	0.0442	1.0000					
cen2	-0.3303	-0.0615	1.0000				
age2	-0.0451	0.0692	-0.3038	1.0000			
sex2	-0.0041	0.0794	0.0656	0.0013	1.0000		
education	-0.1335	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1279	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1679	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1433	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1229	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0529	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1152	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1479	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0622	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.1804	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0399	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0879	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0881	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.0376	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.0333	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553

w4function	0.0067	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.0267	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4srhealth	-0.0035	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.0593	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.0213	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0139	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.0383	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0210	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n

cognitivea~y	1.0000						
alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
tot	0.1868	0.1640	0.1924	1.0000			
w4physact	0.2583	0.1807	0.1749	0.2924	1.0000		
w4symptom	-0.1835	-0.1758	-0.1076	-0.3523	-0.4082	1.0000	
w4function	-0.2572	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000
w4vol	0.2362	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903
w4srhealth	0.2265	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396
w4cogability	0.5832	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520
w4alc	0.1610	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446
w4dep	-0.1584	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388
w4groupmem	0.1986	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867
w4casp19	0.1802	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917

	w4vol	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4vol	1.0000						
w4srhealth	0.2104	1.0000					
w4cogability	0.2455	0.2585	1.0000				
w4alc	0.1459	0.2169	0.1786	1.0000			
w4dep	-0.1389	-0.4030	-0.1927	-0.1755	1.0000		
w4groupmem	0.4572	0.2151	0.2155	0.2824	-0.1467	1.0000	
w4casp19	0.1796	0.5114	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_w4sr~h	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4srhealth	1.0000						
Pain2	0.0456	1.0000					
cen2	-0.3522	-0.0615	1.0000				
age2	-0.0319	0.0692	-0.3038	1.0000			
sex2	-0.0067	0.0794	0.0656	0.0013	1.0000		
education	-0.1412	-0.1299	0.1479	-0.2689	-0.1542	1.0000	

wealth	-0.1342	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1813	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1459	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1432	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0557	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1231	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1610	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0672	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.2069	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0438	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0885	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.1013	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.1730	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	-0.0814	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.3606	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.1249	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	-0.0059	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4cogability	0.0031	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.1631	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0192	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.1497	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0310	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334

groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n
cognitivea~y	1.0000						
alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
tot	0.1868	0.1640	0.1924	1.0000			
w4physact	0.2583	0.1807	0.1749	0.2924	1.0000		
w4symptom	-0.1835	-0.1758	-0.1076	-0.3523	-0.4082	1.0000	
w4function	-0.2572	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000
w4vol	0.2362	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903
w4smoke	-0.0144	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307
w4cogability	0.5832	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520
w4alc	0.1610	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446
w4dep	-0.1584	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388
w4groupmem	0.1986	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867
w4casp19	0.1802	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917

	w4vol	w4smoke	w4coga~y	w4alc	w4dep	w4grou~m	w4casp19
w4vol	1.0000						
w4smoke	-0.1131	1.0000					

w4cogability	0.2455	-0.0345	1.0000				
w4alc	0.1459	-0.0792	0.1786	1.0000			
w4dep	-0.1389	0.0800	-0.1927	-0.1755	1.0000		
w4groupmem	0.4572	-0.1745	0.2155	0.2824	-0.1467	1.0000	
w4casp19	0.1796	-0.1122	0.2105	0.1696	-0.4561	0.2110	1.0000

	m_w4co~y	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4cogabi~y	1.0000						
Pain2	0.0453	1.0000					
cen2	-0.3540	-0.0615	1.0000				
age2	-0.0288	0.0692	-0.3038	1.0000			
sex2	-0.0068	0.0794	0.0656	0.0013	1.0000		
education	-0.1426	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1373	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1838	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1467	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1431	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0545	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1248	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1621	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0671	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.2090	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0451	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0889	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.1007	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.1818	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	-0.0633	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.3580	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.1257	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	-0.0065	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.0236	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4alc	-0.1703	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0147	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248

w4groupmem	-0.1556	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0357	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n
cognitivea~y	1.0000						
alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
tot	0.1868	0.1640	0.1924	1.0000			
w4physact	0.2583	0.1807	0.1749	0.2924	1.0000		

w4symptom	-0.1835	-0.1758	-0.1076	-0.3523	-0.4082	1.0000	
w4function	-0.2572	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000
w4vol	0.2362	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903
w4smoke	-0.0144	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307
w4srhealth	0.2265	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396
w4alc	0.1610	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446
w4dep	-0.1584	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388
w4groupmem	0.1986	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867
w4casp19	0.1802	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917

	w4vol	w4smoke	w4srhe~h	w4alc	w4dep	w4grou~m	w4casp19
w4vol	1.0000						
w4smoke	-0.1131	1.0000					
w4srhealth	0.2104	-0.1211	1.0000				
w4alc	0.1459	-0.0792	0.2169	1.0000			
w4dep	-0.1389	0.0800	-0.4030	-0.1755	1.0000		
w4groupmem	0.4572	-0.1745	0.2151	0.2824	-0.1467	1.0000	
w4casp19	0.1796	-0.1122	0.5114	0.1696	-0.4561	0.2110	1.0000

	m_w4alc	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4alc	1.0000						
Pain2	0.0475	1.0000					
cen2	-0.3245	-0.0615	1.0000				
age2	-0.0407	0.0692	-0.3038	1.0000			
sex2	-0.0035	0.0794	0.0656	0.0013	1.0000		
education	-0.1430	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1351	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1721	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1387	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1203	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0513	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1118	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199

hehelf	-0.1529	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0706	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.1879	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0509	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0871	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0888	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.0617	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.0470	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.0261	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.0470	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	-0.0084	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.0570	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.0986	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4dep	0.0254	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.0113	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0411	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174

w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n
cognitivea~y	1.0000						
alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
tot	0.1868	0.1640	0.1924	1.0000			
w4physact	0.2583	0.1807	0.1749	0.2924	1.0000		
w4symptom	-0.1835	-0.1758	-0.1076	-0.3523	-0.4082	1.0000	
w4function	-0.2572	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000
w4vol	0.2362	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903
w4smoke	-0.0144	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307
w4srhealth	0.2265	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396
w4cogability	0.5832	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520
w4dep	-0.1584	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388
w4groupmem	0.1986	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867
w4casp19	0.1802	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917

	w4vol	w4smoke	w4srhe~h	w4coga~y	w4dep	w4grou~m	w4casp19
w4vol	1.0000						
w4smoke	-0.1131	1.0000					
w4srhealth	0.2104	-0.1211	1.0000				
w4cogability	0.2455	-0.0345	0.2585	1.0000			
w4dep	-0.1389	0.0800	-0.4030	-0.1927	1.0000		
w4groupmem	0.4572	-0.1745	0.2151	0.2155	-0.1467	1.0000	
w4casp19	0.1796	-0.1122	0.5114	0.2105	-0.4561	0.2110	1.0000

	m_w4dep	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4dep	1.0000						
Pain2	0.0476	1.0000					
cen2	-0.3528	-0.0615	1.0000				
age2	-0.0266	0.0692	-0.3038	1.0000			
sex2	-0.0069	0.0794	0.0656	0.0013	1.0000		
education	-0.1409	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1380	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1861	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1507	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1495	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0550	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1184	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1688	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0725	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.2112	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0448	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0889	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.1118	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.1723	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	-0.0512	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.3338	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.1062	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	-0.0001	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.0679	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.0657	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.1564	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4groupmem	-0.1515	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169
w4casp19	-0.0801	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						

```
symptomcount |  -0.4302   1.0000
    function |  -0.4586   0.6330   1.0000
       smoke |  -0.0898   0.0605   0.0548   1.0000
volunteerw~k |   0.1790  -0.1572  -0.1548  -0.1019   1.0000
      hehelf |   0.4010  -0.4896  -0.4521  -0.1365   0.1831   1.0000
         dep |  -0.2502   0.3456   0.3358   0.0705  -0.1114  -0.3694   1.0000
cognitivea~y |   0.2555  -0.2164  -0.2124  -0.0399   0.1667   0.2406  -0.1498
         alc |   0.1693  -0.1749  -0.1609   0.0332   0.0578   0.1800  -0.1334
    groupmem |   0.2066  -0.1269  -0.1213  -0.1321   0.3689   0.1653  -0.1013
         tot |   0.3254  -0.4203  -0.4205  -0.1107   0.1556   0.4946  -0.4144
   w4physact |   0.4955  -0.3741  -0.3713  -0.1037   0.1568   0.3641  -0.2203
   w4symptom |  -0.3448   0.5781   0.4665   0.1035  -0.1259  -0.4425   0.2953
  w4function |  -0.3641   0.4616   0.6061   0.0457  -0.1312  -0.3676   0.2434
       w4vol |   0.1968  -0.1532  -0.1557  -0.1270   0.4751   0.1804  -0.1174
     w4smoke |  -0.0850   0.0820   0.0701   0.6205  -0.0939  -0.1259   0.0904
  w4srhealth |   0.3293  -0.4043  -0.3770  -0.1459   0.1316   0.6283  -0.3088
w4cogability |   0.2177  -0.2020  -0.1807  -0.0621   0.1604   0.2079  -0.1462
       w4alc |   0.1916  -0.1981  -0.1814   0.0024   0.0811   0.1990  -0.1427
  w4groupmem |   0.2408  -0.1603  -0.1481  -0.1700   0.3838   0.2160  -0.1263
     w4casp19 |   0.2718  -0.3465  -0.3317  -0.1100   0.1247   0.4354  -0.3439


             | cognit~y      alc groupmem      tot w4phys~t w4symp~m w4func~n
-------------+------------------------------------------------------------
cognitivea~y |   1.0000
         alc |   0.1248   1.0000
    groupmem |   0.1113   0.1321   1.0000
         tot |   0.1868   0.1640   0.1924   1.0000
   w4physact |   0.2583   0.1807   0.1749   0.2924   1.0000
   w4symptom |  -0.1835  -0.1758  -0.1076  -0.3523  -0.4082   1.0000
  w4function |  -0.2572  -0.1572  -0.0850  -0.3393  -0.4680   0.4652   1.0000
       w4vol |   0.2362   0.0961   0.3600   0.1745   0.2554  -0.1635  -0.1903
     w4smoke |  -0.0144  -0.0651  -0.1439  -0.1311  -0.1032   0.0859   0.0307
  w4srhealth |   0.2265   0.1763   0.1400   0.4413   0.4106  -0.5202  -0.4396
w4cogability |   0.5832   0.1205   0.1198   0.1618   0.2829  -0.2429  -0.2520
```

w4alc	0.1610	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446
w4groupmem	0.1986	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867
w4casp19	0.1802	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917

	w4vol	w4smoke	w4srhe~h	w4coga~y	w4alc	w4grou~m	w4casp19
w4vol	1.0000						
w4smoke	-0.1131	1.0000					
w4srhealth	0.2104	-0.1211	1.0000				
w4cogability	0.2455	-0.0345	0.2585	1.0000			
w4alc	0.1459	-0.0792	0.2169	0.1786	1.0000		
w4groupmem	0.4572	-0.1745	0.2151	0.2155	0.2824	1.0000	
w4casp19	0.1796	-0.1122	0.5114	0.2105	0.1696	0.2110	1.0000

	m_w4gr~m	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4groupmem	1.0000						
Pain2	0.0527	1.0000					
cen2	-0.3098	-0.0615	1.0000				
age2	-0.0402	0.0692	-0.3038	1.0000			
sex2	0.0051	0.0794	0.0656	0.0013	1.0000		
education	-0.1536	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1408	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.1681	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1455	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1209	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0567	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1255	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1565	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.0722	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.1846	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0585	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.1089	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.0903	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999

w4physact	-0.0606	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.0723	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.0176	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.1106	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	0.0422	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.0635	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.0760	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.0198	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.0483	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4casp19	-0.0418	-0.2925	0.1443	-0.1731	0.0056	0.1832	0.2683

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000
cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4casp19	0.2718	-0.3465	-0.3317	-0.1100	0.1247	0.4354	-0.3439

	cognit~y	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n
cognitivea~y	1.0000						
alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
tot	0.1868	0.1640	0.1924	1.0000			
w4physact	0.2583	0.1807	0.1749	0.2924	1.0000		
w4symptom	-0.1835	-0.1758	-0.1076	-0.3523	-0.4082	1.0000	
w4function	-0.2572	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000
w4vol	0.2362	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903
w4smoke	-0.0144	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307
w4srhealth	0.2265	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396
w4cogability	0.5832	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520
w4alc	0.1610	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446
w4dep	-0.1584	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388
w4casp19	0.1802	0.1590	0.1558	0.7096	0.3211	-0.4019	-0.3917

	w4vol	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4casp19
w4vol	1.0000						
w4smoke	-0.1131	1.0000					
w4srhealth	0.2104	-0.1211	1.0000				
w4cogability	0.2455	-0.0345	0.2585	1.0000			
w4alc	0.1459	-0.0792	0.2169	0.1786	1.0000		
w4dep	-0.1389	0.0800	-0.4030	-0.1927	-0.1755	1.0000	
w4casp19	0.1796	-0.1122	0.5114	0.2105	0.1696	-0.4561	1.0000

	m_w4c~19	Pain2	cen2	age2	sex2	educat~n	wealth
m_w4casp19	1.0000						
Pain2	0.0654	1.0000					
cen2	-0.3207	-0.0615	1.0000				
age2	0.0325	0.0692	-0.3038	1.0000			

sex2	0.0080	0.0794	0.0656	0.0013	1.0000		
education	-0.1727	-0.1299	0.1479	-0.2689	-0.1542	1.0000	
wealth	-0.1829	-0.1706	0.1653	-0.1523	-0.0508	0.4057	1.0000
phact	-0.2148	-0.2480	0.2767	-0.2889	-0.0687	0.2443	0.2821
symptomcount	0.1655	0.3735	-0.2519	0.2414	0.0453	-0.1771	-0.2402
function	0.1691	0.3496	-0.2439	0.2113	0.0546	-0.1470	-0.2166
smoke	0.0649	0.0516	-0.0686	-0.0585	-0.1252	-0.0932	-0.1678
volunteerw~k	-0.1305	-0.0818	0.1177	-0.0762	0.0374	0.2576	0.2199
hehelf	-0.1909	-0.4115	0.2348	-0.1705	0.0083	0.2288	0.2923
dep	0.1044	0.2854	-0.1243	0.1089	0.1295	-0.1816	-0.2160
cognitivea~y	-0.2489	-0.0932	0.2814	-0.4438	0.0898	0.3377	0.2667
alc	-0.0603	-0.1295	0.0818	-0.1267	-0.2121	0.2098	0.2320
groupmem	-0.0916	-0.0801	0.0577	0.0230	0.0049	0.2824	0.2516
tot	-0.1338	-0.3145	0.1849	-0.1193	0.0296	0.1667	0.2999
w4physact	-0.2369	-0.2261	0.2696	-0.3264	-0.0864	0.2446	0.2815
w4symptom	0.0982	0.3604	-0.1675	0.2411	0.0576	-0.1934	-0.2553
w4function	0.2574	0.2406	-0.3181	0.2918	0.0516	-0.1542	-0.1956
w4vol	-0.1484	-0.0874	0.1317	-0.1403	0.0161	0.3207	0.2604
w4smoke	0.0519	0.0586	-0.0240	-0.1209	-0.0003	-0.0991	-0.1907
w4srhealth	-0.1612	-0.3547	0.1637	-0.1844	-0.0163	0.2372	0.2792
w4cogability	-0.2034	-0.1047	0.2381	-0.4596	0.0826	0.3437	0.2499
w4alc	-0.3776	-0.1273	0.1360	-0.1656	-0.1897	0.2321	0.2593
w4dep	0.1213	0.2778	-0.1126	0.1379	0.1317	-0.1856	-0.2248
w4groupmem	-0.3328	-0.1070	0.1253	-0.0535	0.0151	0.3304	0.3169

	phact	sympto~t	function	smoke	volunt~k	hehelf	dep
phact	1.0000						
symptomcount	-0.4302	1.0000					
function	-0.4586	0.6330	1.0000				
smoke	-0.0898	0.0605	0.0548	1.0000			
volunteerw~k	0.1790	-0.1572	-0.1548	-0.1019	1.0000		
hehelf	0.4010	-0.4896	-0.4521	-0.1365	0.1831	1.0000	
dep	-0.2502	0.3456	0.3358	0.0705	-0.1114	-0.3694	1.0000

cognitivea~y	0.2555	-0.2164	-0.2124	-0.0399	0.1667	0.2406	-0.1498
alc	0.1693	-0.1749	-0.1609	0.0332	0.0578	0.1800	-0.1334
groupmem	0.2066	-0.1269	-0.1213	-0.1321	0.3689	0.1653	-0.1013
tot	0.3254	-0.4203	-0.4205	-0.1107	0.1556	0.4946	-0.4144
w4physact	0.4955	-0.3741	-0.3713	-0.1037	0.1568	0.3641	-0.2203
w4symptom	-0.3448	0.5781	0.4665	0.1035	-0.1259	-0.4425	0.2953
w4function	-0.3641	0.4616	0.6061	0.0457	-0.1312	-0.3676	0.2434
w4vol	0.1968	-0.1532	-0.1557	-0.1270	0.4751	0.1804	-0.1174
w4smoke	-0.0850	0.0820	0.0701	0.6205	-0.0939	-0.1259	0.0904
w4srhealth	0.3293	-0.4043	-0.3770	-0.1459	0.1316	0.6283	-0.3088
w4cogability	0.2177	-0.2020	-0.1807	-0.0621	0.1604	0.2079	-0.1462
w4alc	0.1916	-0.1981	-0.1814	0.0024	0.0811	0.1990	-0.1427
w4dep	-0.2306	0.3054	0.3136	0.0792	-0.0928	-0.3247	0.4339
w4groupmem	0.2408	-0.1603	-0.1481	-0.1700	0.3838	0.2160	-0.1263

	cognit~y	alc	groupmem	tot	w4phys~t	w4symp~m	w4func~n
cognitivea~y	1.0000						
alc	0.1248	1.0000					
groupmem	0.1113	0.1321	1.0000				
tot	0.1868	0.1640	0.1924	1.0000			
w4physact	0.2583	0.1807	0.1749	0.2924	1.0000		
w4symptom	-0.1835	-0.1758	-0.1076	-0.3523	-0.4082	1.0000	
w4function	-0.2572	-0.1572	-0.0850	-0.3393	-0.4680	0.4652	1.0000
w4vol	0.2362	0.0961	0.3600	0.1745	0.2554	-0.1635	-0.1903
w4smoke	-0.0144	-0.0651	-0.1439	-0.1311	-0.1032	0.0859	0.0307
w4srhealth	0.2265	0.1763	0.1400	0.4413	0.4106	-0.5202	-0.4396
w4cogability	0.5832	0.1205	0.1198	0.1618	0.2829	-0.2429	-0.2520
w4alc	0.1610	0.6525	0.1198	0.1660	0.2581	-0.1895	-0.2446
w4dep	-0.1584	-0.1353	-0.0975	-0.3725	-0.2827	0.3858	0.3388
w4groupmem	0.1986	0.1384	0.5966	0.2120	0.2814	-0.1526	-0.1867

	w4vol	w4smoke	w4srhe~h	w4coga~y	w4alc	w4dep	w4grou~m

```
       w4vol |   1.0000
     w4smoke |  -0.1131   1.0000
  w4srhealth |   0.2104  -0.1211   1.0000
w4cogability |   0.2455  -0.0345   0.2585   1.0000
       w4alc |   0.1459  -0.0792   0.2169   0.1786   1.0000
       w4dep |  -0.1389   0.0800  -0.4030  -0.1927  -0.1755   1.0000
  w4groupmem |   0.4572  -0.1745   0.2151   0.2155   0.2824  -0.1467   1.0000


.
. log close
      name:  <unnamed>
       log:  S:\Data\ELSAmissing.log
  log type:  text
 closed on:  26 Jun 2015, 10:39:10
```

NorStOP

```
-------------------------------------------------------------------------------------------
---
      name:  <unnamed>
       log:  S:\Data\NORSTOP\NorStOPmissingdata.log
  log type:  text
 opened on:  22 Dec 2014, 10:44:02


. local corrvars "pain numpain censor age sex education income alcohol smoke control health
wa
> lk depression anxiety sleep1 sleep2 sleep3 sleep4 out partic obesity physfunct painint
cogni
> tive slp3 bmi3 pf3 anx3 dep3 cog3 gh3 part3"


.
. foreach var of varlist pain censor age sex education income alcohol smoke control health
wal
> k depression anxiety sleep1 sleep2 sleep3 sleep4 out partic obesity physfunct painint
cognit
> ive slp3 bmi3 pf3 anx3 dep3 cog3 gh3 part3{
  2.
```

```
. gen m_`var' = missing(`var')
  3.
. pwcorr m_`var' `: list corrvars - var'
  4.
. }
```

	m_pain	numpain	censor	age	sex	educat~n	income
m_pain	1.0000						
numpain	-0.0003	1.0000					
censor	0.0466	0.0262	1.0000				
age	0.1254	-0.0068	0.3915	1.0000			
sex	-0.0145	-0.0747	0.0518	-0.0690	1.0000		
education	0.0133	0.0448	0.0574	0.1316	0.0546	1.0000	
income	0.0189	0.1639	0.0205	0.0011	-0.0089	0.0854	1.0000
alcohol	0.0331	0.1042	0.0612	0.1774	-0.2396	0.0480	0.1104
smoke	-0.0089	-0.0282	-0.0447	0.0234	-0.2045	-0.0207	-0.0153
control	0.0355	-0.0253	-0.0355	0.0079	0.0004	-0.0231	-0.0183
health	0.0474	0.4020	0.2056	0.2392	-0.0032	0.1192	0.2131
walk	0.0207	0.2255	0.1543	0.1947	-0.0922	0.0467	0.0898
depression	0.0137	0.2844	0.1168	0.1129	-0.0088	0.0480	0.1843
anxiety	0.0043	0.2686	0.0126	-0.0272	-0.1434	0.0266	0.1966
sleep1	0.0092	0.2471	0.0228	0.0352	-0.1027	0.0326	0.1366
sleep2	-0.0152	0.2151	0.0735	0.0713	-0.0598	0.0371	0.1028
sleep3	0.0017	0.2480	0.0230	0.0142	-0.0818	0.0269	0.1277
sleep4	-0.0014	0.3014	0.0247	-0.0337	-0.0705	0.0200	0.1580
out	0.0491	0.2502	0.2320	0.3669	-0.1078	0.1013	0.1423
partic	0.0636	0.2308	0.1396	0.1966	-0.0606	0.0759	0.1802
obesity	-0.0151	0.1349	-0.0401	-0.1006	-0.0384	0.0088	0.0809
physfunct	-0.0414	-0.4878	-0.2653	-0.3937	0.1320	-0.1142	-0.2186
painint	0.0013	0.5589	0.1571	0.1977	-0.0374	0.0939	0.2139
cognitive	0.0114	0.2688	0.1076	0.1484	-0.0455	0.0247	0.1619
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.

pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	alcohol	smoke	control	health	walk	depres~n	anxiety
alcohol	1.0000						
smoke	0.1158	1.0000					
control	0.0002	-0.1999	1.0000				
health	0.1598	-0.0613	-0.0208	1.0000			
walk	0.1398	-0.0122	-0.0217	0.3826	1.0000		
depression	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000	
anxiety	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194	1.0000
sleep1	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458	0.2644
sleep2	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141	0.2287
sleep3	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595	0.2775
sleep4	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434	0.3157
out	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932	0.2236
partic	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266	0.2428
obesity	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809	0.0592
physfunct	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536	-0.3021
painint	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082	0.3212
cognitive	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					
cognitive	-0.3703	0.3374	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.

```
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             | m_censor     pain  numpain      age      sex educat~n   income
-------------+------------------------------------------------------------------
    m_censor |   1.0000
        pain |   0.0116   1.0000
     numpain |  -0.0072  -0.5166   1.0000
         age |   0.3003   0.0064  -0.0068   1.0000
         sex |   0.0086   0.0328  -0.0747  -0.0690   1.0000
   education |   0.0395  -0.0491   0.0448   0.1316   0.0546   1.0000
      income |   0.0132  -0.1015   0.1639   0.0011  -0.0089   0.0854   1.0000
     alcohol |   0.0613  -0.0345   0.1042   0.1774  -0.2396   0.0480   0.1104
       smoke |  -0.0093   0.0179  -0.0282   0.0234  -0.2045  -0.0207  -0.0153
     control |  -0.0096   0.0340  -0.0253   0.0079   0.0004  -0.0231  -0.0183
      health |   0.1619  -0.2913   0.4020   0.2392  -0.0032   0.1192   0.2131
        walk |   0.1226  -0.1561   0.2255   0.1947  -0.0922   0.0467   0.0898
  depression |   0.1189  -0.1664   0.2844   0.1129  -0.0088   0.0480   0.1843
     anxiety |   0.0212  -0.2060   0.2686  -0.0272  -0.1434   0.0266   0.1966
      sleep1 |   0.0124  -0.1532   0.2471   0.0352  -0.1027   0.0326   0.1366
      sleep2 |   0.0466  -0.1648   0.2151   0.0713  -0.0598   0.0371   0.1028
      sleep3 |   0.0146  -0.1675   0.2480   0.0142  -0.0818   0.0269   0.1277
      sleep4 |   0.0210  -0.1813   0.3014  -0.0337  -0.0705   0.0200   0.1580
         out |   0.1881  -0.1554   0.2502   0.3669  -0.1078   0.1013   0.1423
      partic |   0.1265  -0.1608   0.2308   0.1966  -0.0606   0.0759   0.1802
     obesity |  -0.0361  -0.0988   0.1349  -0.1006  -0.0384   0.0088   0.0809
   physfunct |  -0.1836   0.3525  -0.4878  -0.3937   0.1320  -0.1142  -0.2186
     painint |   0.1062  -0.4996   0.5589   0.1977  -0.0374   0.0939   0.2139
```

cognitive	0.0773	-0.1985	0.2688	0.1484	-0.0455	0.0247	0.1619
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	alcohol	smoke	control	health	walk	depres~n	anxiety
alcohol	1.0000						
smoke	0.1158	1.0000					
control	0.0002	-0.1999	1.0000				
health	0.1598	-0.0613	-0.0208	1.0000			
walk	0.1398	-0.0122	-0.0217	0.3826	1.0000		
depression	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000	
anxiety	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194	1.0000
sleep1	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458	0.2644
sleep2	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141	0.2287
sleep3	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595	0.2775
sleep4	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434	0.3157
out	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932	0.2236
partic	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266	0.2428
obesity	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809	0.0592
physfunct	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536	-0.3021
painint	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082	0.3212
cognitive	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.

cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					
cognitive	-0.3703	0.3374	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.

dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	dep3	cog3	gh3	part3
dep3	.			
cog3	.	.		
gh3	.	.	.	
part3	.	.	.	.

	m_age	pain	numpain	censor	sex	educat~n	income
m_age	1.0000						
pain	.	1.0000					
numpain	-0.0003	-0.5166	1.0000				
censor	.	-0.0124	0.0262	1.0000			
sex	.	0.0328	-0.0747	0.0518	1.0000		
education	.	-0.0491	0.0448	0.0574	0.0546	1.0000	
income	.	-0.1015	0.1639	0.0205	-0.0089	0.0854	1.0000
alcohol	-0.0035	-0.0345	0.1042	0.0612	-0.2396	0.0480	0.1104
smoke	0.0011	0.0179	-0.0282	-0.0447	-0.2045	-0.0207	-0.0153
control	0.0049	0.0340	-0.0253	-0.0355	0.0004	-0.0231	-0.0183
health	0.0144	-0.2913	0.4020	0.2056	-0.0032	0.1192	0.2131
walk	0.0014	-0.1561	0.2255	0.1543	-0.0922	0.0467	0.0898
depression	.	-0.1664	0.2844	0.1168	-0.0088	0.0480	0.1843
anxiety	.	-0.2060	0.2686	0.0126	-0.1434	0.0266	0.1966
sleep1	0.0098	-0.1532	0.2471	0.0228	-0.1027	0.0326	0.1366
sleep2	0.0080	-0.1648	0.2151	0.0735	-0.0598	0.0371	0.1028
sleep3	-0.0001	-0.1675	0.2480	0.0230	-0.0818	0.0269	0.1277
sleep4	-0.0061	-0.1813	0.3014	0.0247	-0.0705	0.0200	0.1580
out	0.0055	-0.1554	0.2502	0.2320	-0.1078	0.1013	0.1423
partic	0.0077	-0.1608	0.2308	0.1396	-0.0606	0.0759	0.1802

obesity	-0.0168	-0.0988	0.1349	-0.0401	-0.0384	0.0088	0.0809
physfunct	.	0.3525	-0.4878	-0.2653	0.1320	-0.1142	-0.2186
painint	.	-0.4996	0.5589	0.1571	-0.0374	0.0939	0.2139
cognitive	.	-0.1985	0.2688	0.1076	-0.0455	0.0247	0.1619
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	alcohol	smoke	control	health	walk	depres~n	anxiety
alcohol	1.0000						
smoke	0.1158	1.0000					
control	0.0002	-0.1999	1.0000				
health	0.1598	-0.0613	-0.0208	1.0000			
walk	0.1398	-0.0122	-0.0217	0.3826	1.0000		
depression	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000	
anxiety	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194	1.0000
sleep1	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458	0.2644
sleep2	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141	0.2287
sleep3	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595	0.2775
sleep4	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434	0.3157
out	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932	0.2236
partic	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266	0.2428
obesity	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809	0.0592
physfunct	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536	-0.3021
painint	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082	0.3212
cognitive	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.

pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					
cognitive	-0.3703	0.3374	1.0000				
slp3	.	.	.	.			

```
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             |    m_sex     pain  numpain   censor      age educat~n   income
-------------+---------------------------------------------------------------
       m_sex |   1.0000
        pain |        .   1.0000
     numpain |  -0.0003  -0.5166   1.0000
      censor |        .  -0.0124   0.0262   1.0000
         age |        .   0.0064  -0.0068   0.3915   1.0000
   education |        .  -0.0491   0.0448   0.0574   0.1316   1.0000
      income |        .  -0.1015   0.1639   0.0205   0.0011   0.0854   1.0000
     alcohol |  -0.0035  -0.0345   0.1042   0.0612   0.1774   0.0480   0.1104
       smoke |   0.0011   0.0179  -0.0282  -0.0447   0.0234  -0.0207  -0.0153
     control |   0.0049   0.0340  -0.0253  -0.0355   0.0079  -0.0231  -0.0183
      health |   0.0144  -0.2913   0.4020   0.2056   0.2392   0.1192   0.2131
        walk |   0.0014  -0.1561   0.2255   0.1543   0.1947   0.0467   0.0898
  depression |        .  -0.1664   0.2844   0.1168   0.1129   0.0480   0.1843
     anxiety |        .  -0.2060   0.2686   0.0126  -0.0272   0.0266   0.1966
      sleep1 |   0.0098  -0.1532   0.2471   0.0228   0.0352   0.0326   0.1366
      sleep2 |   0.0080  -0.1648   0.2151   0.0735   0.0713   0.0371   0.1028
      sleep3 |  -0.0001  -0.1675   0.2480   0.0230   0.0142   0.0269   0.1277
```

sleep4	-0.0061	-0.1813	0.3014	0.0247	-0.0337	0.0200	0.1580
out	0.0055	-0.1554	0.2502	0.2320	0.3669	0.1013	0.1423
partic	0.0077	-0.1608	0.2308	0.1396	0.1966	0.0759	0.1802
obesity	-0.0168	-0.0988	0.1349	-0.0401	-0.1006	0.0088	0.0809
physfunct	.	0.3525	-0.4878	-0.2653	-0.3937	-0.1142	-0.2186
painint	.	-0.4996	0.5589	0.1571	0.1977	0.0939	0.2139
cognitive	.	-0.1985	0.2688	0.1076	0.1484	0.0247	0.1619
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	alcohol	smoke	control	health	walk	depres~n	anxiety
alcohol	1.0000						
smoke	0.1158	1.0000					
control	0.0002	-0.1999	1.0000				
health	0.1598	-0.0613	-0.0208	1.0000			
walk	0.1398	-0.0122	-0.0217	0.3826	1.0000		
depression	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000	
anxiety	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194	1.0000
sleep1	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458	0.2644
sleep2	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141	0.2287
sleep3	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595	0.2775
sleep4	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434	0.3157
out	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932	0.2236
partic	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266	0.2428
obesity	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809	0.0592
physfunct	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536	-0.3021
painint	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082	0.3212

cognitive	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						

```
     painint |  -0.7328   1.0000
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             | m_educ~n     pain  numpain   censor      age      sex   income
-------------+---------------------------------------------------------------
 m_education |   1.0000
        pain |   0.0008   1.0000
     numpain |   0.0008  -0.5166   1.0000
      censor |   0.0373  -0.0124   0.0262   1.0000
         age |   0.0740   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0236   0.0328  -0.0747   0.0518  -0.0690   1.0000
      income |   0.0107  -0.1015   0.1639   0.0205   0.0011  -0.0089   1.0000
     alcohol |   0.0331  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.1104
       smoke |   0.0141   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0153
     control |   0.0010   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0183
      health |   0.0316  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.2131
        walk |  -0.0020  -0.1561   0.2255   0.1543   0.1947  -0.0922   0.0898
  depression |   0.0252  -0.1664   0.2844   0.1168   0.1129  -0.0088   0.1843
     anxiety |   0.0065  -0.2060   0.2686   0.0126  -0.0272  -0.1434   0.1966
```

sleep1	0.0208	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.1366
sleep2	0.0156	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.1028
sleep3	0.0137	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.1277
sleep4	0.0023	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.1580
out	0.0350	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1423
partic	0.0399	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.1802
obesity	-0.0054	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0809
physfunct	-0.0339	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.2186
painint	0.0227	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.2139
cognitive	0.0273	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.1619
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	alcohol	smoke	control	health	walk	depres~n	anxiety
alcohol	1.0000						
smoke	0.1158	1.0000					
control	0.0002	-0.1999	1.0000				
health	0.1598	-0.0613	-0.0208	1.0000			
walk	0.1398	-0.0122	-0.0217	0.3826	1.0000		
depression	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000	
anxiety	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194	1.0000
sleep1	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458	0.2644
sleep2	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141	0.2287
sleep3	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595	0.2775
sleep4	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434	0.3157
out	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932	0.2236
partic	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266	0.2428

obesity	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809	0.0592
physfunct	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536	-0.3021
painint	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082	0.3212
cognitive	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					
cognitive	-0.3703	0.3374	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	dep3	cog3	gh3	part3
dep3	.			
cog3	.	.		
gh3	.	.	.	
part3	.	.	.	.

	m_income	pain	numpain	censor	age	sex	educat~n
m_income	1.0000						
pain	-0.0116	1.0000					
numpain	0.0092	-0.5166	1.0000				
censor	0.0495	-0.0124	0.0262	1.0000			
age	0.0807	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0033	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	-0.0002	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
alcohol	0.0360	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	0.0019	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	0.0108	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0643	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192

walk	0.0231	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0465	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0282	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0449	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0310	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0349	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0299	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0589	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0683	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	0.0027	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0593	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0507	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0445	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	alcohol	smoke	control	health	walk	depres~n	anxiety
alcohol	1.0000						
smoke	0.1158	1.0000					
control	0.0002	-0.1999	1.0000				
health	0.1598	-0.0613	-0.0208	1.0000			
walk	0.1398	-0.0122	-0.0217	0.3826	1.0000		
depression	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000	
anxiety	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194	1.0000
sleep1	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458	0.2644
sleep2	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141	0.2287
sleep3	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595	0.2775

sleep4	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434	0.3157
out	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932	0.2236
partic	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266	0.2428
obesity	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809	0.0592
physfunct	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536	-0.3021
painint	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082	0.3212
cognitive	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.

```
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .


             | physfu~t  painint cognit~e     slp3     bmi3      pf3     anx3
-------------+------------------------------------------------------------------
   physfunct |   1.0000
     painint |  -0.7328   1.0000
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .


             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .


             | m_alco~l     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
   m_alcohol |   1.0000
        pain |  -0.0052   1.0000
     numpain |   0.0015  -0.5166   1.0000
      censor |   0.0379  -0.0124   0.0262   1.0000
         age |   0.0469   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0065   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0002  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |  -0.0029  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
```

smoke	0.0059	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	-0.0052	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0285	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	-0.0057	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0049	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	-0.0046	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0066	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0010	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0018	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0013	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0214	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0254	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0006	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0214	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0141	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0129	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	smoke	control	health	walk	depres~n	anxiety
income	1.0000						
smoke	-0.0153	1.0000					
control	-0.0183	-0.1999	1.0000				
health	0.2131	-0.0613	-0.0208	1.0000			
walk	0.0898	-0.0122	-0.0217	0.3826	1.0000		
depression	0.1843	-0.0228	-0.0093	0.4413	0.2985	1.0000	
anxiety	0.1966	0.0093	-0.0463	0.3234	0.1692	0.4194	1.0000

sleep1	0.1366	0.0159	-0.0210	0.2494	0.1541	0.2458	0.2644
sleep2	0.1028	0.0773	-0.2186	0.2480	0.1485	0.2141	0.2287
sleep3	0.1277	0.0020	-0.0150	0.2533	0.1502	0.2595	0.2775
sleep4	0.1580	-0.0090	-0.0167	0.3126	0.1934	0.3434	0.3157
out	0.1423	-0.0011	-0.0112	0.4615	0.5116	0.3932	0.2236
partic	0.1802	-0.0131	0.0373	0.3890	0.2798	0.3266	0.2428
obesity	0.0809	-0.0148	-0.0148	0.1423	0.1125	0.0809	0.0592
physfunct	-0.2186	0.0236	0.0378	-0.6629	-0.5167	-0.4536	-0.3021
painint	0.2139	-0.0337	-0.0276	0.5991	0.3743	0.4082	0.3212
cognitive	0.1619	-0.0113	-0.0263	0.3374	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.

```
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             | physfu~t  painint cognit~e     slp3     bmi3      pf3     anx3
-------------+------------------------------------------------------------------
   physfunct |   1.0000
     painint |  -0.7328   1.0000
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             |  m_smoke     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
     m_smoke |   1.0000
        pain |  -0.0090   1.0000
     numpain |  -0.0037  -0.5166   1.0000
      censor |   0.0226  -0.0124   0.0262   1.0000
         age |   0.0617   0.0064  -0.0068   0.3915   1.0000
```

sex	-0.0023	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0053	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0030	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0170	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
control	0.0068	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0241	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0046	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0108	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0034	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0021	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0027	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	-0.0008	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	-0.0037	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0150	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0352	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0043	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0293	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0168	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0211	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	control	health	walk	depres~n	anxiety
income	1.0000						
alcohol	0.1104	1.0000					
control	-0.0183	0.0002	1.0000				
health	0.2131	0.1598	-0.0208	1.0000			

walk	0.0898	0.1398	-0.0217	0.3826	1.0000		
depression	0.1843	0.1205	-0.0093	0.4413	0.2985	1.0000	
anxiety	0.1966	0.0856	-0.0463	0.3234	0.1692	0.4194	1.0000
sleep1	0.1366	0.0943	-0.0210	0.2494	0.1541	0.2458	0.2644
sleep2	0.1028	0.0764	-0.2186	0.2480	0.1485	0.2141	0.2287
sleep3	0.1277	0.0701	-0.0150	0.2533	0.1502	0.2595	0.2775
sleep4	0.1580	0.0853	-0.0167	0.3126	0.1934	0.3434	0.3157
out	0.1423	0.1925	-0.0112	0.4615	0.5116	0.3932	0.2236
partic	0.1802	0.1316	0.0373	0.3890	0.2798	0.3266	0.2428
obesity	0.0809	0.0709	-0.0148	0.1423	0.1125	0.0809	0.0592
physfunct	-0.2186	-0.2143	0.0378	-0.6629	-0.5167	-0.4536	-0.3021
painint	0.2139	0.1430	-0.0276	0.5991	0.3743	0.4082	0.3212
cognitive	0.1619	0.0893	-0.0263	0.3374	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497

```
        slp3 |        .        .        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             | physfu~t  painint cognit~e     slp3     bmi3      pf3     anx3
-------------+------------------------------------------------------------------
   physfunct |   1.0000
     painint |  -0.7328   1.0000
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             | m_cont~l     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
   m_control |   1.0000
        pain |  -0.0109   1.0000
```

numpain	0.0002	-0.5166	1.0000				
censor	0.0436	-0.0124	0.0262	1.0000			
age	0.0784	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0281	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	-0.0061	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0144	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0377	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	0.0132	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
health	0.0498	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0334	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0373	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0134	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0204	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	-0.0061	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0006	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0127	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0439	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0403	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0084	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0592	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0377	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0117	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	health	walk	depres~n	anxiety
income	1.0000						

alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
health	0.2131	0.1598	-0.0613	1.0000			
walk	0.0898	0.1398	-0.0122	0.3826	1.0000		
depression	0.1843	0.1205	-0.0228	0.4413	0.2985	1.0000	
anxiety	0.1966	0.0856	0.0093	0.3234	0.1692	0.4194	1.0000
sleep1	0.1366	0.0943	0.0159	0.2494	0.1541	0.2458	0.2644
sleep2	0.1028	0.0764	0.0773	0.2480	0.1485	0.2141	0.2287
sleep3	0.1277	0.0701	0.0020	0.2533	0.1502	0.2595	0.2775
sleep4	0.1580	0.0853	-0.0090	0.3126	0.1934	0.3434	0.3157
out	0.1423	0.1925	-0.0011	0.4615	0.5116	0.3932	0.2236
partic	0.1802	0.1316	-0.0131	0.3890	0.2798	0.3266	0.2428
obesity	0.0809	0.0709	-0.0148	0.1423	0.1125	0.0809	0.0592
physfunct	-0.2186	-0.2143	0.0236	-0.6629	-0.5167	-0.4536	-0.3021
painint	0.2139	0.1430	-0.0337	0.5991	0.3743	0.4082	0.3212
cognitive	0.1619	0.0893	-0.0113	0.3374	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000

physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					
cognitive	-0.3703	0.3374	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	dep3	cog3	gh3	part3
dep3	.			
cog3	.	.		
gh3	.	.	.	
part3	.	.	.	.

	m_health	pain	numpain	censor	age	sex	educat~n

m_health	1.0000						
pain	-0.0034	1.0000					
numpain	0.0112	-0.5166	1.0000				
censor	0.0191	-0.0124	0.0262	1.0000			
age	0.0479	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0144	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0070	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0185	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0278	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	0.0091	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	-0.0122	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
walk	-0.0016	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0164	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0171	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0058	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	-0.0032	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	-0.0005	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	-0.0025	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0176	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0178	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0009	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0290	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0163	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0015	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	walk	depres~n	anxiety
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
walk	0.0898	0.1398	-0.0122	-0.0217	1.0000		
depression	0.1843	0.1205	-0.0228	-0.0093	0.2985	1.0000	
anxiety	0.1966	0.0856	0.0093	-0.0463	0.1692	0.4194	1.0000
sleep1	0.1366	0.0943	0.0159	-0.0210	0.1541	0.2458	0.2644
sleep2	0.1028	0.0764	0.0773	-0.2186	0.1485	0.2141	0.2287
sleep3	0.1277	0.0701	0.0020	-0.0150	0.1502	0.2595	0.2775
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.1934	0.3434	0.3157
out	0.1423	0.1925	-0.0011	-0.0112	0.5116	0.3932	0.2236
partic	0.1802	0.1316	-0.0131	0.0373	0.2798	0.3266	0.2428
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1125	0.0809	0.0592
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.5167	-0.4536	-0.3021
painint	0.2139	0.1430	-0.0337	-0.0276	0.3743	0.4082	0.3212
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.1898	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			

out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					
cognitive	-0.3703	0.3374	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	dep3	cog3	gh3	part3
dep3	.			
cog3	.	.		
gh3	.	.	.	

part3	.	.	.	.			

	m_walk	pain	numpain	censor	age	sex	educat~n
m_walk	1.0000						
pain	0.0100	1.0000					
numpain	-0.0158	-0.5166	1.0000				
censor	0.0256	-0.0124	0.0262	1.0000			
age	0.0533	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0125	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0200	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0058	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0242	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	-0.0007	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	-0.0047	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0124	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
depression	0.0088	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	-0.0018	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0162	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0110	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0003	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	-0.0020	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	-0.0022	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0189	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0101	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0160	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0145	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0109	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.

gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	depres~n	anxiety
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	1.0000	
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.4194	1.0000
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.2458	0.2644
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.2141	0.2287
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.2595	0.2775
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.3434	0.3157
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.3932	0.2236
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.3266	0.2428
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.0809	0.0592
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.4536	-0.3021
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.4082	0.3212
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.3500	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						

```
      sleep2 |   0.4145   1.0000
      sleep3 |   0.5954   0.5615   1.0000
      sleep4 |   0.4645   0.3710   0.5106   1.0000
         out |   0.1898   0.1781   0.1792   0.2070   1.0000
      partic |   0.1729   0.1439   0.1654   0.2007   0.3858   1.0000
     obesity |   0.0710   0.0755   0.0821   0.0925   0.0588   0.0663   1.0000
   physfunct |  -0.2685  -0.2789  -0.2762  -0.3075  -0.5691  -0.4574  -0.1629
     painint |   0.2669   0.2630   0.2840   0.3106   0.4388   0.4100   0.1405
   cognitive |   0.2026   0.2101   0.2179   0.2623   0.2751   0.2715   0.0497
        slp3 |        .        .        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             | physfu~t  painint cognit~e     slp3     bmi3      pf3     anx3
-------------+------------------------------------------------------------------
   physfunct |   1.0000
     painint |  -0.7328   1.0000
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
```

```
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             | m_depr~n     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
m_depression |   1.0000
        pain |  -0.0031   1.0000
     numpain |  -0.0036  -0.5166   1.0000
      censor |   0.0258  -0.0124   0.0262   1.0000
         age |   0.0533   0.0064  -0.0068   0.3915   1.0000
         sex |   0.0022   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0064  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |   0.0095  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0161  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
       smoke |   0.0002   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0207
     control |   0.0075   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0231
      health |   0.0332  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.1192
        walk |   0.0163  -0.1561   0.2255   0.1543   0.1947  -0.0922   0.0467
     anxiety |  -0.0004  -0.2060   0.2686   0.0126  -0.0272  -0.1434   0.0266
      sleep1 |   0.0174  -0.1532   0.2471   0.0228   0.0352  -0.1027   0.0326
      sleep2 |   0.0134  -0.1648   0.2151   0.0735   0.0713  -0.0598   0.0371
      sleep3 |   0.0210  -0.1675   0.2480   0.0230   0.0142  -0.0818   0.0269
      sleep4 |   0.0043  -0.1813   0.3014   0.0247  -0.0337  -0.0705   0.0200
         out |   0.0308  -0.1554   0.2502   0.2320   0.3669  -0.1078   0.1013
      partic |   0.0350  -0.1608   0.2308   0.1396   0.1966  -0.0606   0.0759
     obesity |  -0.0128  -0.0988   0.1349  -0.0401  -0.1006  -0.0384   0.0088
   physfunct |  -0.0353   0.3525  -0.4878  -0.2653  -0.3937   0.1320  -0.1142
     painint |   0.0309  -0.4996   0.5589   0.1571   0.1977  -0.0374   0.0939
   cognitive |   0.0302  -0.1985   0.2688   0.1076   0.1484  -0.0455   0.0247
        slp3 |        .        .        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
```

anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	anxiety
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	1.0000
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2644
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2287
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2775
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3157
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.2236
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.2428
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0592
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.3021
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.3212
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3471
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					
cognitive	-0.3703	0.3374	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	dep3	cog3	gh3	part3
dep3	.			
cog3	.	.		
gh3	.	.	.	
part3	.	.	.	.

	m_anxi~y	pain	numpain	censor	age	sex	educat~n
m_anxiety	1.0000						
pain	-0.0056	1.0000					
numpain	-0.0010	-0.5166	1.0000				
censor	0.0267	-0.0124	0.0262	1.0000			
age	0.0612	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0003	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0062	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0098	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0195	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	0.0017	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	0.0048	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0362	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0160	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0317	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
sleep1	0.0171	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0150	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0192	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0041	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0346	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0374	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0091	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0416	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0333	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0294	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247

slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.

gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	sleep1	sleep2	sleep3	sleep4	out	partic	obesity
sleep1	1.0000						
sleep2	0.4145	1.0000					
sleep3	0.5954	0.5615	1.0000				
sleep4	0.4645	0.3710	0.5106	1.0000			
out	0.1898	0.1781	0.1792	0.2070	1.0000		
partic	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					
cognitive	-0.3703	0.3374	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.

```
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .


             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .


             | m_sleep1     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------
    m_sleep1 |   1.0000
        pain |  -0.0076   1.0000
     numpain |  -0.0245  -0.5166   1.0000
      censor |   0.0234  -0.0124   0.0262   1.0000
         age |   0.0677   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0240   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0101  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |   0.0186  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0423  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
       smoke |   0.0056   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0207
     control |   0.0103   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0231
      health |   0.0242  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.1192
        walk |   0.0137  -0.1561   0.2255   0.1543   0.1947  -0.0922   0.0467
  depression |   0.0120  -0.1664   0.2844   0.1168   0.1129  -0.0088   0.0480
     anxiety |   0.0065  -0.2060   0.2686   0.0126  -0.0272  -0.1434   0.0266
      sleep2 |   0.0268  -0.1648   0.2151   0.0735   0.0713  -0.0598   0.0371
      sleep3 |   0.0271  -0.1675   0.2480   0.0230   0.0142  -0.0818   0.0269
      sleep4 |   0.0075  -0.1813   0.3014   0.0247  -0.0337  -0.0705   0.0200
         out |   0.0298  -0.1554   0.2502   0.2320   0.3669  -0.1078   0.1013
      partic |   0.0530  -0.1608   0.2308   0.1396   0.1966  -0.0606   0.0759
     obesity |   0.0002  -0.0988   0.1349  -0.0401  -0.1006  -0.0384   0.0088
```

physfunct	-0.0238	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0174	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	-0.0114	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.

anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep2	sleep3	sleep4	out	partic	obesity
anxiety	1.0000						
sleep2	0.2287	1.0000					
sleep3	0.2775	0.5615	1.0000				
sleep4	0.3157	0.3710	0.5106	1.0000			
out	0.2236	0.1781	0.1792	0.2070	1.0000		
partic	0.2428	0.1439	0.1654	0.2007	0.3858	1.0000	
obesity	0.0592	0.0755	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.3021	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.3212	0.2630	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.3471	0.2101	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					
cognitive	-0.3703	0.3374	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		

```
        pf3 |        .        .        .        .        .        .
       anx3 |        .        .        .        .        .        .        .
       dep3 |        .        .        .        .        .        .        .
       cog3 |        .        .        .        .        .        .        .
        gh3 |        .        .        .        .        .        .        .
      part3 |        .        .        .        .        .        .        .
```

```
             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
       cog3 |        .        .
        gh3 |        .        .        .
      part3 |        .        .        .        .
```

```
             | m_sleep2     pain  numpain   censor      age      sex educat~n
-------------+---------------------------------------------------------------
    m_sleep2 |   1.0000
        pain |   0.0150   1.0000
     numpain |  -0.0337  -0.5166   1.0000
      censor |   0.0269  -0.0124   0.0262   1.0000
         age |   0.0657   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0066   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |  -0.0011  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |   0.0016  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0196  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
       smoke |   0.0087   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0207
     control |   0.0084   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0231
      health |   0.0020  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.1192
        walk |  -0.0004  -0.1561   0.2255   0.1543   0.1947  -0.0922   0.0467
  depression |  -0.0089  -0.1664   0.2844   0.1168   0.1129  -0.0088   0.0480
     anxiety |  -0.0198  -0.2060   0.2686   0.0126  -0.0272  -0.1434   0.0266
      sleep1 |  -0.0001  -0.1532   0.2471   0.0228   0.0352  -0.1027   0.0326
      sleep3 |   0.0032  -0.1675   0.2480   0.0230   0.0142  -0.0818   0.0269
      sleep4 |  -0.0040  -0.1813   0.3014   0.0247  -0.0337  -0.0705   0.0200
```

out	0.0146	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0314	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0095	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0004	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	-0.0008	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	-0.0173	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500

slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep3	sleep4	out	partic	obesity
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep3	0.2775	0.5954	1.0000				
sleep4	0.3157	0.4645	0.5106	1.0000			
out	0.2236	0.1898	0.1792	0.2070	1.0000		
partic	0.2428	0.1729	0.1654	0.2007	0.3858	1.0000	
obesity	0.0592	0.0710	0.0821	0.0925	0.0588	0.0663	1.0000
physfunct	-0.3021	-0.2685	-0.2762	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.3212	0.2669	0.2840	0.3106	0.4388	0.4100	0.1405
cognitive	0.3471	0.2026	0.2179	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3
physfunct	1.0000						
painint	-0.7328	1.0000					

```
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             | m_sleep3     pain  numpain   censor      age      sex educat~n
-------------+---------------------------------------------------------------
    m_sleep3 |   1.0000
        pain |   0.0043   1.0000
     numpain |  -0.0317  -0.5166   1.0000
      censor |   0.0330  -0.0124   0.0262   1.0000
         age |   0.0882   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0357   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0036  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |   0.0101  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0365  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
       smoke |   0.0162   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0207
     control |   0.0054   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0231
      health |   0.0135  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.1192
        walk |   0.0079  -0.1561   0.2255   0.1543   0.1947  -0.0922   0.0467
  depression |   0.0001  -0.1664   0.2844   0.1168   0.1129  -0.0088   0.0480
     anxiety |  -0.0236  -0.2060   0.2686   0.0126  -0.0272  -0.1434   0.0266
```

sleep1	-0.0090	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	-0.0016	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep4	0.0010	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0274	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0513	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0001	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0170	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0031	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	-0.0280	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809

physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep4	out	partic	obesity
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep4	0.3157	0.4645	0.3710	1.0000			
out	0.2236	0.1898	0.1781	0.2070	1.0000		
partic	0.2428	0.1729	0.1439	0.2007	0.3858	1.0000	
obesity	0.0592	0.0710	0.0755	0.0925	0.0588	0.0663	1.0000
physfunct	-0.3021	-0.2685	-0.2789	-0.3075	-0.5691	-0.4574	-0.1629
painint	0.3212	0.2669	0.2630	0.3106	0.4388	0.4100	0.1405
cognitive	0.3471	0.2026	0.2101	0.2623	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	physfu~t	painint	cognit~e	slp3	bmi3	pf3	anx3

```
-------------+------------------------------------------------------------

   physfunct |   1.0000
     painint |  -0.7328   1.0000
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .


             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .


             | m_sleep4     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
    m_sleep4 |   1.0000
        pain |   0.0132   1.0000
     numpain |  -0.0387  -0.5166   1.0000
      censor |   0.0357  -0.0124   0.0262   1.0000
         age |   0.0825   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0209   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0040  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |  -0.0009  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0316  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
       smoke |   0.0152   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0207
     control |   0.0132   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0231
      health |   0.0066  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.1192
```

walk	0.0005	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	-0.0011	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	-0.0283	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0029	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0013	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0163	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
out	0.0194	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0451	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0075	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0034	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	-0.0018	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	-0.0337	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595

out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	out	partic	obesity
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
out	0.2236	0.1898	0.1781	0.1792	1.0000		
partic	0.2428	0.1729	0.1439	0.1654	0.3858	1.0000	
obesity	0.0592	0.0710	0.0755	0.0821	0.0588	0.0663	1.0000
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.5691	-0.4574	-0.1629
painint	0.3212	0.2669	0.2630	0.2840	0.4388	0.4100	0.1405
cognitive	0.3471	0.2026	0.2101	0.2179	0.2751	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.

```
       part3 |        .        .        .        .        .        .        .

             | physfu~t  painint cognit~e     slp3     bmi3      pf3     anx3
-------------+------------------------------------------------------------------
   physfunct |   1.0000
     painint |  -0.7328   1.0000
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             |    m_out     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
       m_out |   1.0000
        pain |   0.0035   1.0000
     numpain |  -0.0025  -0.5166   1.0000
      censor |   0.0395  -0.0124   0.0262   1.0000
         age |   0.0696   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0183   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0158  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |   0.0179  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0271  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
```

smoke	0.0074	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	-0.0035	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0389	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0285	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0319	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0088	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0111	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0112	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0045	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0040	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
partic	0.0386	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0089	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0385	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0401	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0161	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194

sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	partic	obesity
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
partic	0.2428	0.1729	0.1439	0.1654	0.2007	1.0000	
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0663	1.0000
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.4574	-0.1629
painint	0.3212	0.2669	0.2630	0.2840	0.3106	0.4100	0.1405
cognitive	0.3471	0.2026	0.2101	0.2179	0.2623	0.2715	0.0497
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.

```
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             | physfu~t  painint cognit~e     slp3     bmi3      pf3     anx3
-------------+------------------------------------------------------------------
   physfunct |   1.0000
     painint |  -0.7328   1.0000
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             | m_partic     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
    m_partic |   1.0000
        pain |   0.0248   1.0000
     numpain |  -0.0456  -0.5166   1.0000
      censor |  -0.0420  -0.0124   0.0262   1.0000
         age |  -0.0153   0.0064  -0.0068   0.3915   1.0000
         sex |   0.0380   0.0328  -0.0747   0.0518  -0.0690   1.0000
```

education	0.0181	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	-0.0149	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	-0.0101	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	-0.0784	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	0.2141	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	-0.0534	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	-0.0392	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	-0.0306	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	-0.0385	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	-0.0381	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	-0.0976	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	-0.0375	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	-0.0337	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	-0.0374	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
obesity	-0.0237	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	0.0769	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	-0.0762	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	-0.0504	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		

walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	obesity
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	1.0000
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.1629
painint	0.3212	0.2669	0.2630	0.2840	0.3106	0.4388	0.1405
cognitive	0.3471	0.2026	0.2101	0.2179	0.2623	0.2751	0.0497
slp3	.	.	.	.	.	.	.

```
        bmi3 |        .        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             | physfu~t  painint cognit~e     slp3     bmi3      pf3     anx3
-------------+------------------------------------------------------------------
   physfunct |   1.0000
     painint |  -0.7328   1.0000
   cognitive |  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .
        bmi3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             | m_obes~y     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
   m_obesity |   1.0000
        pain |   0.0028   1.0000
     numpain |  -0.0034  -0.5166   1.0000
```

censor	0.0462	-0.0124	0.0262	1.0000			
age	0.1012	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0542	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0104	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0333	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0606	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	0.0295	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	-0.0089	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0549	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0470	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0508	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0156	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0197	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0184	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0075	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0110	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0727	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0649	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
physfunct	-0.0636	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0242	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0422	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					

smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574

```
    painint |   0.3212   0.2669   0.2630   0.2840   0.3106   0.4388   0.4100
  cognitive |   0.3471   0.2026   0.2101   0.2179   0.2623   0.2751   0.2715
       slp3 |        .        .        .        .        .        .        .
       bmi3 |        .        .        .        .        .        .        .
        pf3 |        .        .        .        .        .        .        .
       anx3 |        .        .        .        .        .        .        .
       dep3 |        .        .        .        .        .        .        .
       cog3 |        .        .        .        .        .        .        .
        gh3 |        .        .        .        .        .        .        .
      part3 |        .        .        .        .        .        .        .

             | physfu~t  painint cognit~e     slp3     bmi3      pf3     anx3
-------------+------------------------------------------------------------------
  physfunct |   1.0000
    painint |  -0.7328   1.0000
  cognitive |  -0.3703   0.3374   1.0000
       slp3 |        .        .        .        .
       bmi3 |        .        .        .        .        .
        pf3 |        .        .        .        .        .        .
       anx3 |        .        .        .        .        .        .        .
       dep3 |        .        .        .        .        .        .        .
       cog3 |        .        .        .        .        .        .        .
        gh3 |        .        .        .        .        .        .        .
      part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
       dep3 |        .
       cog3 |        .        .
        gh3 |        .        .        .
      part3 |        .        .        .        .

             | m_phys~t     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
```

m_physfunct	1.0000						
pain	-0.0038	1.0000					
numpain	-0.0203	-0.5166	1.0000				
censor	0.0399	-0.0124	0.0262	1.0000			
age	0.1272	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0570	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0078	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0372	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0595	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	0.0335	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	0.0066	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0530	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0307	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0376	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0207	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0433	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0264	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0232	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0196	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0492	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0721	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0021	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
painint	0.0270	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0219	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n

income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		

out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663
painint	0.3212	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100
cognitive	0.3471	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	obesity	painint	cognit~e	slp3	bmi3	pf3	anx3
obesity	1.0000						
painint	0.1405	1.0000					
cognitive	0.0497	0.3374	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	dep3	cog3	gh3	part3
dep3	.			
cog3	.	.		
gh3	.	.	.	
part3	.	.	.	.

	m_pain~t	pain	numpain	censor	age	sex	educat~n
m_painint	1.0000						
pain	0.0121	1.0000					
numpain	-0.0150	-0.5166	1.0000				
censor	0.0320	-0.0124	0.0262	1.0000			
age	0.0738	0.0064	-0.0068	0.3915	1.0000		
sex	0.0066	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0034	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0158	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0215	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	-0.0088	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	-0.0050	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0407	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0143	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0353	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0005	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0127	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0047	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0044	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0054	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0428	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0575	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0100	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0381	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
cognitive	0.0104	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.

part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depression
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic
anxiety	1.0000						
sleep1	0.2644	1.0000					

sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574
cognitive	0.3471	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	obesity	physfu~t	cognit~e	slp3	bmi3	pf3	anx3
obesity	1.0000						
physfunct	-0.1629	1.0000					
cognitive	0.0497	-0.3703	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	dep3	cog3	gh3	part3
dep3	.			

cog3	.	.					
gh3	.	.	.				
part3	.	.	.	.			

	m_cogn~e	pain	numpain	censor	age	sex	educat~n
m_cognitive	1.0000						
pain	-0.0314	1.0000					
numpain	0.0293	-0.5166	1.0000				
censor	0.0568	-0.0124	0.0262	1.0000			
age	0.1326	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0559	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0090	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0356	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0548	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	0.0183	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	0.0052	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.0776	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0506	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0681	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0657	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0509	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0311	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0406	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0429	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.0919	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.0999	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0003	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.0969	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0682	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.

dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic

anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574
painint	0.3212	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	obesity	physfu~t	painint	slp3	bmi3	pf3	anx3
obesity	1.0000						
physfunct	-0.1629	1.0000					
painint	0.1405	-0.7328	1.0000				
slp3	.	.	.	.			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	dep3	cog3	gh3	part3
dep3	.			
cog3	.	.		
gh3	.	.	.	
part3	.	.	.	.

	m_slp3	pain	numpain	censor	age	sex	educat~n
m_slp3	1.0000						
pain	0.0197	1.0000					
numpain	-0.0275	-0.5166	1.0000				
censor	0.1362	-0.0124	0.0262	1.0000			
age	0.2224	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0279	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0707	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0611	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0842	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	-0.0092	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	0.0388	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.1479	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0854	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.0902	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0410	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0313	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0098	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0172	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0205	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.1592	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.1482	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0167	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.1356	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0749	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0624	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247

bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.

part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574
painint	0.3212	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100
cognitive	0.3471	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	obesity	physfu~t	painint	cognit~e	bmi3	pf3	anx3
obesity	1.0000						
physfunct	-0.1629	1.0000					
painint	0.1405	-0.7328	1.0000				
cognitive	0.0497	-0.3703	0.3374	1.0000			
bmi3	.	.	.	.	.		
pf3	.	.	.	.	.	.	
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.

```
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .


             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .


             |   m_bmi3     pain  numpain   censor      age      sex educat~n
-------------+---------------------------------------------------------------
      m_bmi3 |   1.0000
        pain |   0.0252   1.0000
     numpain |  -0.0321  -0.5166   1.0000
      censor |   0.0415  -0.0124   0.0262   1.0000
         age |   0.2136   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0365   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0260  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |   0.0225  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0655  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
       smoke |   0.0379   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0207
     control |  -0.0353   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0231
      health |   0.0613  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.1192
        walk |   0.0318  -0.1561   0.2255   0.1543   0.1947  -0.0922   0.0467
  depression |   0.0372  -0.1664   0.2844   0.1168   0.1129  -0.0088   0.0480
     anxiety |   0.0146  -0.2060   0.2686   0.0126  -0.0272  -0.1434   0.0266
      sleep1 |   0.0173  -0.1532   0.2471   0.0228   0.0352  -0.1027   0.0326
      sleep2 |   0.0188  -0.1648   0.2151   0.0735   0.0713  -0.0598   0.0371
      sleep3 |   0.0104  -0.1675   0.2480   0.0230   0.0142  -0.0818   0.0269
      sleep4 |  -0.0035  -0.1813   0.3014   0.0247  -0.0337  -0.0705   0.0200
         out |   0.0936  -0.1554   0.2502   0.2320   0.3669  -0.1078   0.1013
      partic |   0.0994  -0.1608   0.2308   0.1396   0.1966  -0.0606   0.0759
     obesity |  -0.1050  -0.0988   0.1349  -0.0401  -0.1006  -0.0384   0.0088
```

physfunct	-0.0709	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0228	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0309	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.

```
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |  anxiety   sleep1   sleep2   sleep3   sleep4      out   partic
-------------+------------------------------------------------------------------
     anxiety |   1.0000
      sleep1 |   0.2644   1.0000
      sleep2 |   0.2287   0.4145   1.0000
      sleep3 |   0.2775   0.5954   0.5615   1.0000
      sleep4 |   0.3157   0.4645   0.3710   0.5106   1.0000
         out |   0.2236   0.1898   0.1781   0.1792   0.2070   1.0000
      partic |   0.2428   0.1729   0.1439   0.1654   0.2007   0.3858   1.0000
     obesity |   0.0592   0.0710   0.0755   0.0821   0.0925   0.0588   0.0663
   physfunct |  -0.3021  -0.2685  -0.2789  -0.2762  -0.3075  -0.5691  -0.4574
     painint |   0.3212   0.2669   0.2630   0.2840   0.3106   0.4388   0.4100
   cognitive |   0.3471   0.2026   0.2101   0.2179   0.2623   0.2751   0.2715
        slp3 |        .        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |  obesity physfu~t  painint cognit~e     slp3      pf3     anx3
-------------+------------------------------------------------------------------
     obesity |   1.0000
   physfunct |  -0.1629   1.0000
     painint |   0.1405  -0.7328   1.0000
   cognitive |   0.0497  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .        .
         pf3 |        .        .        .        .        .        .
```

```
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             |    m_pf3     pain  numpain   censor      age      sex educat~n
-------------+---------------------------------------------------------------
       m_pf3 |   1.0000
        pain |   0.0187   1.0000
     numpain |  -0.0204  -0.5166   1.0000
      censor |   0.1387  -0.0124   0.0262   1.0000
         age |   0.2230   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0251   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0684  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |   0.0664  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0859  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
       smoke |  -0.0131   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0207
     control |   0.0418   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0231
      health |   0.1587  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.1192
        walk |   0.0999  -0.1561   0.2255   0.1543   0.1947  -0.0922   0.0467
  depression |   0.1011  -0.1664   0.2844   0.1168   0.1129  -0.0088   0.0480
     anxiety |   0.0476  -0.2060   0.2686   0.0126  -0.0272  -0.1434   0.0266
      sleep1 |   0.0438  -0.1532   0.2471   0.0228   0.0352  -0.1027   0.0326
      sleep2 |   0.0163  -0.1648   0.2151   0.0735   0.0713  -0.0598   0.0371
      sleep3 |   0.0262  -0.1675   0.2480   0.0230   0.0142  -0.0818   0.0269
      sleep4 |   0.0310  -0.1813   0.3014   0.0247  -0.0337  -0.0705   0.0200
```

out	0.1685	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.1554	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0159	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.1446	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0803	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0672	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500

```
        slp3 |        .        .        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |  anxiety   sleep1   sleep2   sleep3   sleep4      out   partic
-------------+------------------------------------------------------------------
     anxiety |   1.0000
      sleep1 |   0.2644   1.0000
      sleep2 |   0.2287   0.4145   1.0000
      sleep3 |   0.2775   0.5954   0.5615   1.0000
      sleep4 |   0.3157   0.4645   0.3710   0.5106   1.0000
         out |   0.2236   0.1898   0.1781   0.1792   0.2070   1.0000
      partic |   0.2428   0.1729   0.1439   0.1654   0.2007   0.3858   1.0000
     obesity |   0.0592   0.0710   0.0755   0.0821   0.0925   0.0588   0.0663
   physfunct |  -0.3021  -0.2685  -0.2789  -0.2762  -0.3075  -0.5691  -0.4574
     painint |   0.3212   0.2669   0.2630   0.2840   0.3106   0.4388   0.4100
   cognitive |   0.3471   0.2026   0.2101   0.2179   0.2623   0.2751   0.2715
        slp3 |        .        .        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |  obesity physfu~t  painint cognit~e     slp3     bmi3     anx3
-------------+------------------------------------------------------------------
     obesity |   1.0000
   physfunct |  -0.1629   1.0000
     painint |   0.1405  -0.7328   1.0000
```

```
   cognitive |   0.0497  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             |   m_anx3     pain  numpain   censor      age      sex educat~n
-------------+---------------------------------------------------------------
      m_anx3 |   1.0000
        pain |   0.0186   1.0000
     numpain |  -0.0200  -0.5166   1.0000
      censor |   0.1388  -0.0124   0.0262   1.0000
         age |   0.2220   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0249   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0684  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |   0.0665  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0829  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
       smoke |  -0.0146   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0207
     control |   0.0491   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0231
      health |   0.1600  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.1192
        walk |   0.0988  -0.1561   0.2255   0.1543   0.1947  -0.0922   0.0467
  depression |   0.1015  -0.1664   0.2844   0.1168   0.1129  -0.0088   0.0480
     anxiety |   0.0475  -0.2060   0.2686   0.0126  -0.0272  -0.1434   0.0266
      sleep1 |   0.0441  -0.1532   0.2471   0.0228   0.0352  -0.1027   0.0326
```

sleep2	0.0134	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0255	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0306	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.1680	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.1543	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0168	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.1447	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0802	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0687	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809

physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574
painint	0.3212	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100
cognitive	0.3471	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	obesity	physfu~t	painint	cognit~e	slp3	bmi3	pf3

```
     obesity |   1.0000
   physfunct |  -0.1629   1.0000
     painint |   0.1405  -0.7328   1.0000
   cognitive |   0.0497  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     dep3     cog3      gh3    part3
-------------+------------------------------------
        dep3 |        .
        cog3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             |   m_dep3     pain  numpain   censor      age      sex educat~n
-------------+---------------------------------------------------------------
      m_dep3 |   1.0000
        pain |   0.0182   1.0000
     numpain |  -0.0198  -0.5166   1.0000
      censor |   0.1385  -0.0124   0.0262   1.0000
         age |   0.2221   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0251   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0683  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
      income |   0.0664  -0.1015   0.1639   0.0205   0.0011  -0.0089   0.0854
     alcohol |   0.0831  -0.0345   0.1042   0.0612   0.1774  -0.2396   0.0480
       smoke |  -0.0144   0.0179  -0.0282  -0.0447   0.0234  -0.2045  -0.0207
     control |   0.0488   0.0340  -0.0253  -0.0355   0.0079   0.0004  -0.0231
      health |   0.1601  -0.2913   0.4020   0.2056   0.2392  -0.0032   0.1192
        walk |   0.0988  -0.1561   0.2255   0.1543   0.1947  -0.0922   0.0467
```

depression	0.1016	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0477	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0442	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0135	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0257	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0307	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.1680	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.1543	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0167	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.1450	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0804	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0689	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434

out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574
painint	0.3212	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100
cognitive	0.3471	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	obesity	physfu~t	painint	cognit~e	slp3	bmi3	pf3
obesity	1.0000						
physfunct	-0.1629	1.0000					
painint	0.1405	-0.7328	1.0000				
cognitive	0.0497	-0.3703	0.3374	1.0000			
slp3	.	.	.	.	.		
bmi3	.	.	.	.	.	.	
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anx3	cog3	gh3	part3
anx3	.			
cog3	.	.		
gh3	.	.	.	
part3	.	.	.	.

	m_cog3	pain	numpain	censor	age	sex	educat~n
m_cog3	1.0000						
pain	0.0184	1.0000					
numpain	-0.0175	-0.5166	1.0000				
censor	0.1387	-0.0124	0.0262	1.0000			
age	0.2226	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0270	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0665	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0671	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0835	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	-0.0177	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207

control	0.0541	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.1601	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0985	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.1024	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0475	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0434	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0110	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0263	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0334	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.1681	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.1550	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0183	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.1452	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0802	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0703	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458

sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574
painint	0.3212	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100
cognitive	0.3471	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.

```
        dep3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |  obesity physfu~t  painint cognit~e     slp3     bmi3      pf3
-------------+------------------------------------------------------------------
     obesity |   1.0000
   physfunct |  -0.1629   1.0000
     painint |   0.1405  -0.7328   1.0000
   cognitive |   0.0497  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     anx3     dep3      gh3    part3
-------------+------------------------------------
        anx3 |        .
        dep3 |        .        .
         gh3 |        .        .        .
       part3 |        .        .        .        .

             |    m_gh3     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
       m_gh3 |   1.0000
        pain |   0.0197   1.0000
     numpain |  -0.0203  -0.5166   1.0000
      censor |   0.1402  -0.0124   0.0262   1.0000
         age |   0.2220   0.0064  -0.0068   0.3915   1.0000
         sex |  -0.0266   0.0328  -0.0747   0.0518  -0.0690   1.0000
   education |   0.0682  -0.0491   0.0448   0.0574   0.1316   0.0546   1.0000
```

income	0.0665	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0843	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	-0.0138	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	0.0424	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.1592	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0973	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.1016	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0487	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0425	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0166	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0242	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0296	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.1674	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.1555	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0163	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.1436	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0793	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0664	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				
control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	

depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
part3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574
painint	0.3212	0.2669	0.2630	0.2840	0.3106	0.4388	0.4100
cognitive	0.3471	0.2026	0.2101	0.2179	0.2623	0.2751	0.2715
slp3	.	.	.	.	.	.	.

```
        bmi3 |        .        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |  obesity physfu~t  painint cognit~e     slp3     bmi3      pf3
-------------+------------------------------------------------------------------
     obesity |   1.0000
   physfunct |  -0.1629   1.0000
     painint |   0.1405  -0.7328   1.0000
   cognitive |   0.0497  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
       part3 |        .        .        .        .        .        .        .

             |     anx3     dep3     cog3    part3
-------------+------------------------------------
        anx3 |        .
        dep3 |        .        .
        cog3 |        .        .        .
       part3 |        .        .        .        .

             |  m_part3     pain  numpain   censor      age      sex educat~n
-------------+------------------------------------------------------------------
     m_part3 |   1.0000
        pain |   0.0187   1.0000
     numpain |  -0.0196  -0.5166   1.0000
      censor |   0.1375  -0.0124   0.0262   1.0000
```

age	0.2220	0.0064	-0.0068	0.3915	1.0000		
sex	-0.0256	0.0328	-0.0747	0.0518	-0.0690	1.0000	
education	0.0661	-0.0491	0.0448	0.0574	0.1316	0.0546	1.0000
income	0.0668	-0.1015	0.1639	0.0205	0.0011	-0.0089	0.0854
alcohol	0.0844	-0.0345	0.1042	0.0612	0.1774	-0.2396	0.0480
smoke	-0.0193	0.0179	-0.0282	-0.0447	0.0234	-0.2045	-0.0207
control	0.0564	0.0340	-0.0253	-0.0355	0.0079	0.0004	-0.0231
health	0.1598	-0.2913	0.4020	0.2056	0.2392	-0.0032	0.1192
walk	0.0991	-0.1561	0.2255	0.1543	0.1947	-0.0922	0.0467
depression	0.1028	-0.1664	0.2844	0.1168	0.1129	-0.0088	0.0480
anxiety	0.0470	-0.2060	0.2686	0.0126	-0.0272	-0.1434	0.0266
sleep1	0.0440	-0.1532	0.2471	0.0228	0.0352	-0.1027	0.0326
sleep2	0.0095	-0.1648	0.2151	0.0735	0.0713	-0.0598	0.0371
sleep3	0.0261	-0.1675	0.2480	0.0230	0.0142	-0.0818	0.0269
sleep4	0.0315	-0.1813	0.3014	0.0247	-0.0337	-0.0705	0.0200
out	0.1675	-0.1554	0.2502	0.2320	0.3669	-0.1078	0.1013
partic	0.1559	-0.1608	0.2308	0.1396	0.1966	-0.0606	0.0759
obesity	-0.0163	-0.0988	0.1349	-0.0401	-0.1006	-0.0384	0.0088
physfunct	-0.1453	0.3525	-0.4878	-0.2653	-0.3937	0.1320	-0.1142
painint	0.0810	-0.4996	0.5589	0.1571	0.1977	-0.0374	0.0939
cognitive	0.0686	-0.1985	0.2688	0.1076	0.1484	-0.0455	0.0247
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.

	income	alcohol	smoke	control	health	walk	depres~n
income	1.0000						
alcohol	0.1104	1.0000					
smoke	-0.0153	0.1158	1.0000				

control	-0.0183	0.0002	-0.1999	1.0000			
health	0.2131	0.1598	-0.0613	-0.0208	1.0000		
walk	0.0898	0.1398	-0.0122	-0.0217	0.3826	1.0000	
depression	0.1843	0.1205	-0.0228	-0.0093	0.4413	0.2985	1.0000
anxiety	0.1966	0.0856	0.0093	-0.0463	0.3234	0.1692	0.4194
sleep1	0.1366	0.0943	0.0159	-0.0210	0.2494	0.1541	0.2458
sleep2	0.1028	0.0764	0.0773	-0.2186	0.2480	0.1485	0.2141
sleep3	0.1277	0.0701	0.0020	-0.0150	0.2533	0.1502	0.2595
sleep4	0.1580	0.0853	-0.0090	-0.0167	0.3126	0.1934	0.3434
out	0.1423	0.1925	-0.0011	-0.0112	0.4615	0.5116	0.3932
partic	0.1802	0.1316	-0.0131	0.0373	0.3890	0.2798	0.3266
obesity	0.0809	0.0709	-0.0148	-0.0148	0.1423	0.1125	0.0809
physfunct	-0.2186	-0.2143	0.0236	0.0378	-0.6629	-0.5167	-0.4536
painint	0.2139	0.1430	-0.0337	-0.0276	0.5991	0.3743	0.4082
cognitive	0.1619	0.0893	-0.0113	-0.0263	0.3374	0.1898	0.3500
slp3	.	.	.	.	.	.	.
bmi3	.	.	.	.	.	.	.
pf3	.	.	.	.	.	.	.
anx3	.	.	.	.	.	.	.
dep3	.	.	.	.	.	.	.
cog3	.	.	.	.	.	.	.
gh3	.	.	.	.	.	.	.

	anxiety	sleep1	sleep2	sleep3	sleep4	out	partic
anxiety	1.0000						
sleep1	0.2644	1.0000					
sleep2	0.2287	0.4145	1.0000				
sleep3	0.2775	0.5954	0.5615	1.0000			
sleep4	0.3157	0.4645	0.3710	0.5106	1.0000		
out	0.2236	0.1898	0.1781	0.1792	0.2070	1.0000	
partic	0.2428	0.1729	0.1439	0.1654	0.2007	0.3858	1.0000
obesity	0.0592	0.0710	0.0755	0.0821	0.0925	0.0588	0.0663
physfunct	-0.3021	-0.2685	-0.2789	-0.2762	-0.3075	-0.5691	-0.4574

```
     painint |   0.3212   0.2669   0.2630   0.2840   0.3106   0.4388   0.4100
   cognitive |   0.3471   0.2026   0.2101   0.2179   0.2623   0.2751   0.2715
        slp3 |        .        .        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .

             |  obesity physfu~t  painint cognit~e     slp3     bmi3      pf3
-------------+------------------------------------------------------------------
     obesity |   1.0000
   physfunct |  -0.1629   1.0000
     painint |   0.1405  -0.7328   1.0000
   cognitive |   0.0497  -0.3703   0.3374   1.0000
        slp3 |        .        .        .        .        .
        bmi3 |        .        .        .        .        .        .
         pf3 |        .        .        .        .        .        .        .
        anx3 |        .        .        .        .        .        .        .
        dep3 |        .        .        .        .        .        .        .
        cog3 |        .        .        .        .        .        .        .
         gh3 |        .        .        .        .        .        .        .

             |     anx3     dep3     cog3      gh3
-------------+------------------------------------
        anx3 |        .
        dep3 |        .        .
        cog3 |        .        .        .
         gh3 |        .        .        .        .


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Appendix IV - Weighted survival analyses

Table AIV.1. Risk of all-cause mortality in the ELSA complete case sample according to pain phenotype (n=6324) and weighted results										
Pain phenotype	**N**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**	**Weighted Model 1 MRR (95% CI)**	**Weighted Model 2 MRR (95% CI)**	**Weighted Model 3 MRR (95% CI)**
Not often troubled	4052	28048	428	15.26	Reference	Reference	Reference	Reference	Reference	Reference
Often troubled	2272	15414	336	21.80	**1.43 (1.24, 1.65)**	**1.36 (1.18, 1.58)**	**1.29 (1.12, 1.49)**	**1.43 (1.24, 1.65)**	**1.37 (1.18, 1.58)**	**1.29 (1.11, 1.50)**
Not often troubled	4052	28048	428	15.26	Reference	Reference	Reference	Reference	Reference	Reference
Mild	680	4737	60	12.67	0.83 (0.63, 1.09)	0.87 (0.66, 1.14)	0.89 (0.68, 1.16)	0.82 (0.63, 1.08)	0.85 (0.65, 1.12)	0.87 (0.67, 1.14)
Moderate	1183	7943	201	25.31	**1.65 (1.40, 1.95)**	**1.52 (1.28, 1.80)**	**1.42 (1.20, 1.68)**	**1.68 (1.42, 1.98)**	**1.54 (1.30, 1.84)**	**1.43 (1.20, 1.72)**
Severe	409	2734	75	27.43	**1.81 (1.41, 2.31)**	**1.70 (1.33, 2.18)**	**1.54 (1.20, 1.97)**	**1.80 (1.41, 2.31)**	**1.70 (1.31, 2.19)**	**1.53 (1.19, 1.98)**

MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1: Crude
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, education and wealth
***per 1000 person-years**
MRRs in bold indicate significant associations

Table AIV.2. Risk of all-cause mortality in the NorStOP complete case sample according to pain phenotype (n=10985) and weighted results										
Pain phenotype	**N**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**	**Weighted Model 1 MRR (95% CI)**	**Weighted Model 2 MRR (95% CI)**	**Weighted Model 3 MRR (95% CI)**
No pain	3166	28813	412	14.30	Reference	Reference	Reference	Reference	Reference	Reference
Any pain	7819	71116	1072	15.07	1.05 (0.94, 1.18)	1.08 (0.96, 1.21)	1.06 (0.95, 1.19)	1.00 (0.89, 1.12)	1.08 (0.96, 1.20)	1.06 (0.95, 1.19)
No pain	3166	28813	412	14.30	Reference	Reference	Reference	Reference	Reference	Reference
Pain but not ACR WP	5038	45709	714	15.62	1.09 (0.97, 1.23)	1.06 (0.94, 1.20)	1.05 (0.93, 1.19)	1.06 (0.94, 1.19)	1.07 (0.95, 1.20)	1.06 (0.94, 1.19)
ACR WP	2749	25158	352	13.99	0.97 (0.85, 1.12)	1.10 (0.95, 1.26)	1.07 (0.92, 1.23)	0.90 (0.78, 1.04)	1.09 (0.95, 1.26)	1.07 (0.92, 1.23)
No pain	3166	28813	412	14.30	Reference	Reference	Reference	Reference	Reference	Reference
Pain but not Manchester WP	6062	55194	827	14.98	1.05 (0.93, 1.18)	1.05 (0.93, 1.18)	1.03 (0.92, 1.16)	1.02 (0.90, 1.14)	1.05 (0.93, 1.18)	1.04 (0.92, 1.17)
Manchester WP	1725	15673	239	15.25	1.06 (0.91, 1.25)	**1.19 (1.02, 1.40)**	1.16 (0.99, 1.36)	0.94 (0.80, 1.11)	**1.19 (1.01, 1.39)**	1.16 (0.99, 1.36)
No sites	3166	28813	412	14.30	Reference	Reference	Reference	Reference	Reference	Reference
1-3 sites	1952	17843	245	13.73	0.96 (0.82, 1.12)	0.95 (0.81, 1.11)	0.95 (0.81, 1.11)	0.95 (0.81, 1.11)	0.94 (0.81, 1.10)	0.94 (0.80, 1.10)
4-6 sites	1942	17559	276	15.72	1.10 (0.94, 1.28)	1.09 (0.94, 1.27)	1.08 (0.93, 1.26)	1.07 (0.92, 1.24)	1.09 (0.93, 1.26)	1.07 (0.92, 1.25)
7-11 sites	1833	16836	241	14.31	1.00 (0.85, 1.17)	1.07 (0.92, 1.26)	1.05 (0.90, 1.24)	0.94 (0.80, 1.10)	1.06 (0.91, 1.25)	1.05 (0.89, 1.23)
12+ sites	2060	18630	304	16.32	1.14 (0.98, 1.32)	**1.18 (1.02, 1.37)**	1.15 (0.99, 1.34)	1.01 (0.87, 1.17)	**1.17 (1.01, 1.36)**	1.14 (0.99, 1.33)

MRR= Mortality Rate Ratio, 95% CI = 95% confidence interval, ACR = American College of Rheumatology, WP = Widespread pain
Model 1: Crude, Model 2: Adjusted for age, sex, Model 3: Adjusted for age, sex, education, adequacy of income
***per 1000 person-years, MRRs in bold indicate significant associations**

Table AIV.3. Risk of all-cause mortality in the ELSA sample with predictor, outcome and confounder information according to pain phenotype (n=8572)							
Pain phenotype	**N (total =8572)**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
Not often troubled	5322	36145	775	21.44	Reference	Reference	Reference
Often troubled	3250	21624	615	28.44	**1.33 (1.19, 1.47)**	**1.25 (1.13, 1.39)**	**1.18 (1.06, 1.31)**
Not often troubled	5322	36145	775	21.44	Reference	Reference	Reference
Mild	882	5997	118	19.68	0.92 (0.76, 1.11)	0.95 (0.78, 1.16)	0.96 (0.79, 1.17)
Moderate	1698	11271	340	30.17	**1.40 (1.23, 1.59)**	**1.31 (1.16, 1.50)**	**1.23 (1.08, 1.40)**
Severe	670	4356	157	36.04	**1.69 (1.42, 2.01)**	**1.46 (1.23, 1.73)**	**1.30 (1.09, 1.55)**

MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1 Crude
Model 2 Age, sex
Model 3 Age, sex, education, wealth
***per 1000 person-years**

Table AIV.4 Risk of all-cause mortality in the NorStOP baseline sample (with predictor, outcome and confounder information) according to pain phenotype (n=14023)							
Pain phenotype	**N (14023)**	**Person years of follow up**	**Number of deaths**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
No pain	4016	36272	556	15.33	Reference	Reference	Reference
Any pain	10007	90394	1434	15.86	1.03 (0.94, 1.14)	1.07 (0.97, 1.18)	1.06 (0.96, 1.17)
No pain	4016	36272	556	15.33	Reference	Reference	Reference
Pain but not ACR	6483	58302	953	16.35	1.06 (0.96, 1.18)	1.06 (0.95, 1.17)	1.05 (0.94, 1.16)
ACR	3524	32092	481	14.99	0.97 (0.86, 1.10)	1.10 (0.98, 1.25)	1.08 (0.96, 1.22)
No pain	4016	36272	556	15.33	Reference	Reference	Reference
Pain but not Manchester definition	7812	70473	1121	15.91	1.04 (0.94, 1.15)	1.04 (0.94, 1.16)	1.04 (0.93, 1.15)
Manchester definition	2195	19921	313	15.71	1.02 (0.89, 1.17)	**1.18 (1.03, 1.36)**	**1.16 (1.01, 1.33)**
No sites	4062	36615	566	15.46	Reference	Reference	Reference
1-3 sites	2562	23235	335	14.42	0.93 (0.81, 1.06)	0.94 (0.82, 1.08)	0.94 (0.82, 1.07)
4-6 sites	2459	22112	360	16.28	1.05 (0.92, 1.20)	1.07 (0.93, 1.22)	1.06 (0.93, 1.21)
7-11 sites	2330	21220	320	15.08	0.97 (0.85, 1.11)	1.04 (0.91, 1.19)	1.03 (0.89, 1.18)
12+ sites	2610	23484	409	17.42	1.12 (0.99, 1.27)	**1.21 (1.06, 1.37)**	**1.19 (1.04, 1.35)**

MRR= Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1 Crude
Model 2 Age, sex
Model 3 Age, sex, education, adequacy of income
***per 1000 person-years**

Table AIV.5 Risk of all-cause mortality in the NorStOP baseline sample (with predictor, outcome and confounder information) according to pain interference (n=14023)							
Pain interference	**N (14023)**	**Person years of follow up**	**Number of deaths (1990)**	**Mortality rate***	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
No interference	4648	42740	419	9.80	Reference	Reference	Reference
A little	3622	33177	414	12.48	**1.27 (1.11, 1.46)**	**1.14 (1.00, 1.31)**	**1.14 (1.00, 1.31)**
Moderately	2246	20148	398	19.75	**2.02 (1.76, 2.31)**	**1.49 (1.30, 1.71)**	**1.48 (1.29, 1.71)**
Quite a bit	2719	24053	534	22.20	**2.27 (2.00, 2.58)**	**1.67 (1.46, 1.90)**	**1.67 (1.46, 1.90)**
Extremely	788	6549	225	34.36	**3.53 (3.00, 4.15)**	**2.62 (2.22, 3.08)**	**2.63 (2.22, 3.10)**

MRR= Mortality Rate Ratio, 95% CI = 95% confidence interval
Model 1 Crude
Model 2 Age, sex
Model 3 Age, sex, education, adequacy of income
***per 1000 person-years**

Appendix V - Schoenfeld tests and residual plots

Results from the English Longitudinal Study of Ageing (ELSA)

Instructions on how to perform the tests can be found at:
http://www.ats.ucla.edu/stat/examples/asa/test_proportionality.htm

Table AV.1. Results of Schoenfeld tests for baseline sample for those often troubled with pain (n=6324)			
	chi2	**df**	**p**
Often troubled with pain	2.87	1	0.0904
Age	1.50	1	0.2205
Sex	1.26	1	0.2610
Education	1.28	1	0.2585
Wealth	0.01	1	0.9188
Global test	8.13	5	0.1492
df=degrees of freedom			

Figure AV.1. Plot of Schoenfeld residuals for baseline sample (n=6324) comparing those often troubled with pain to those not often troubled

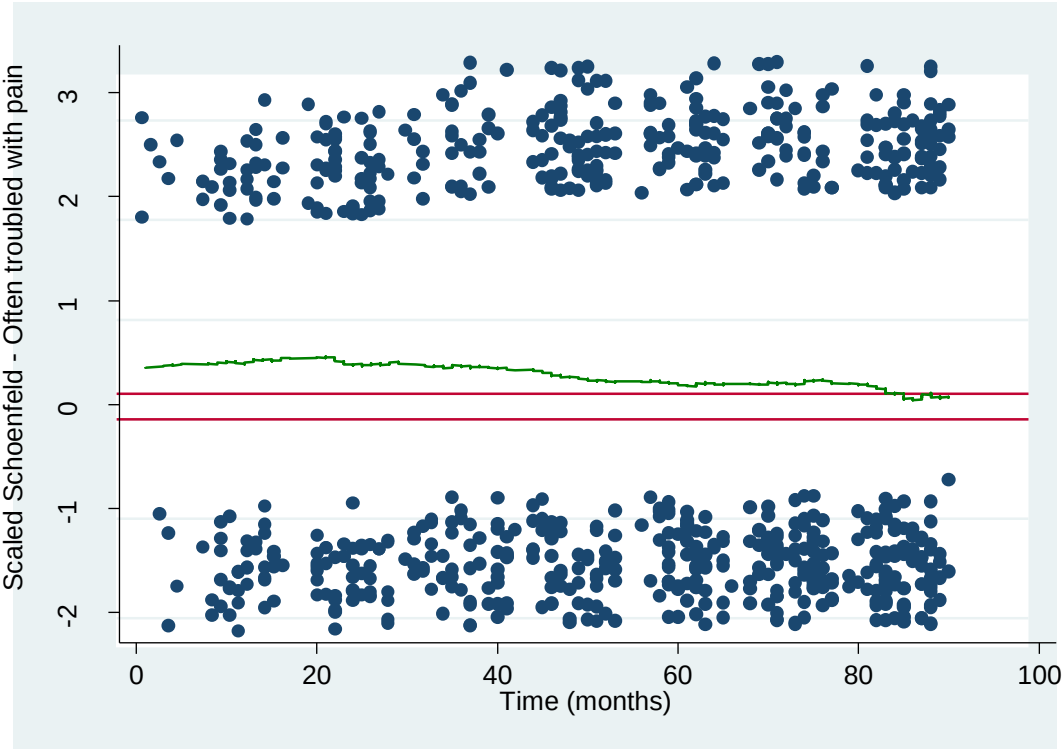
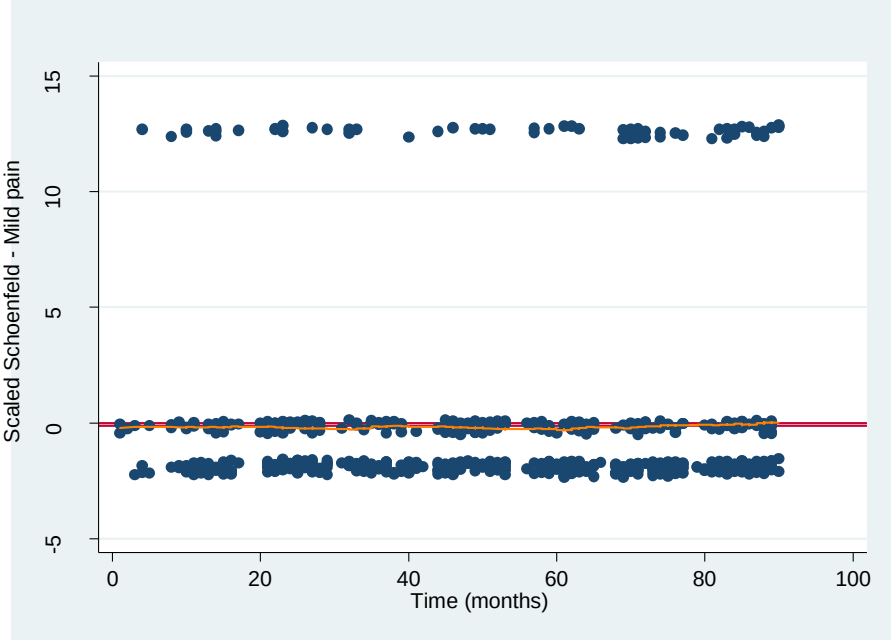


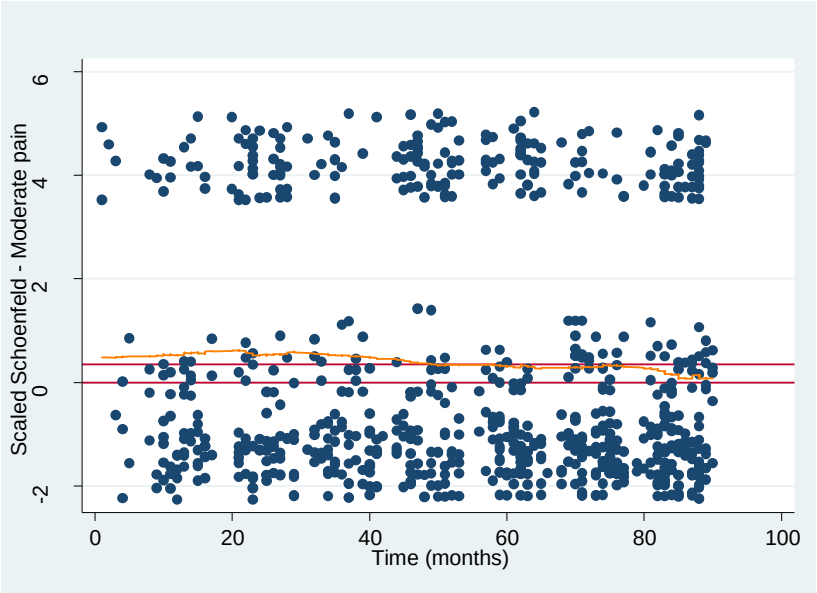
Table AV.2. Results of Schoenfeld tests for baseline sample according to severity of pain (n=6324)			
	Chi2	**df**	**p**
Mild pain	0.04	1	0.8514
Moderate pain	3.33	1	0.0682
Severe pain	1.82	1	0.1772
Age	1.39	1	0.2378
Sex	1.39	1	0.2390
Education	1.54	1	0.2143
Wealth	0.00	1	0.9853
Global test	9.82	7	0.1992
df=degrees of freedom			

Figures AV.2 a-c. Plots of Schoenfeld residuals for baseline sample (n=6324) according to severity of pain

a) Mild pain



b) Moderate pain



c) Severe pain

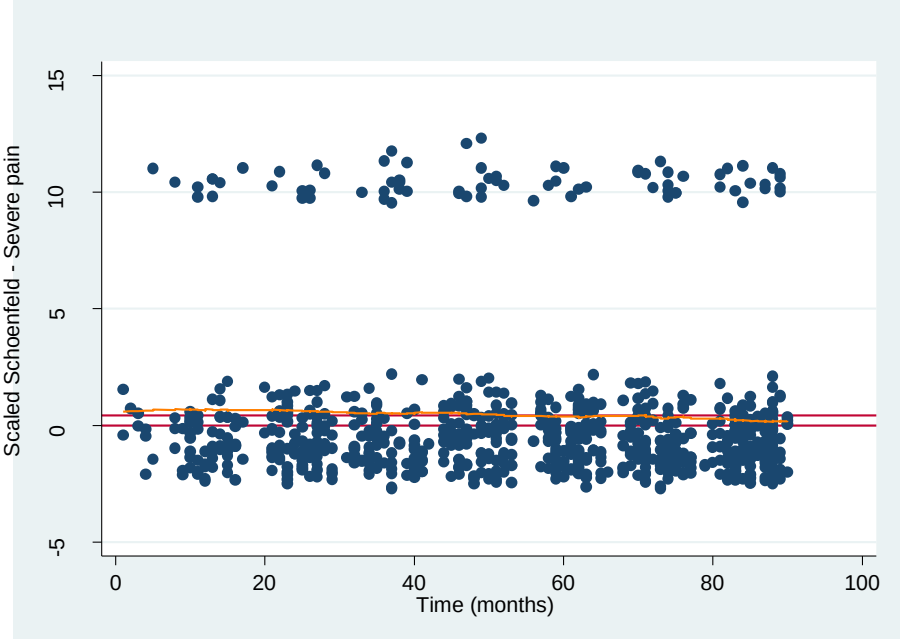


Table AV.3. Results of Schoenfeld tests for baseline complete case sample for those reporting any pain (n=10985)			
	Chi2	**df**	**p**
Any Pain	3.09	1	0.0786
Age	2.50	1	0.1140
Sex	1.42	1	0.2326
Education	1.86	1	0.1723
Adequacy of income	0.34	1	0.5585
Global test	9.63	5	0.0863
df=degrees of freedom			

Figure AV.3. Plot of Schoenfeld residuals for baseline complete case sample (n=10953) according to pain report

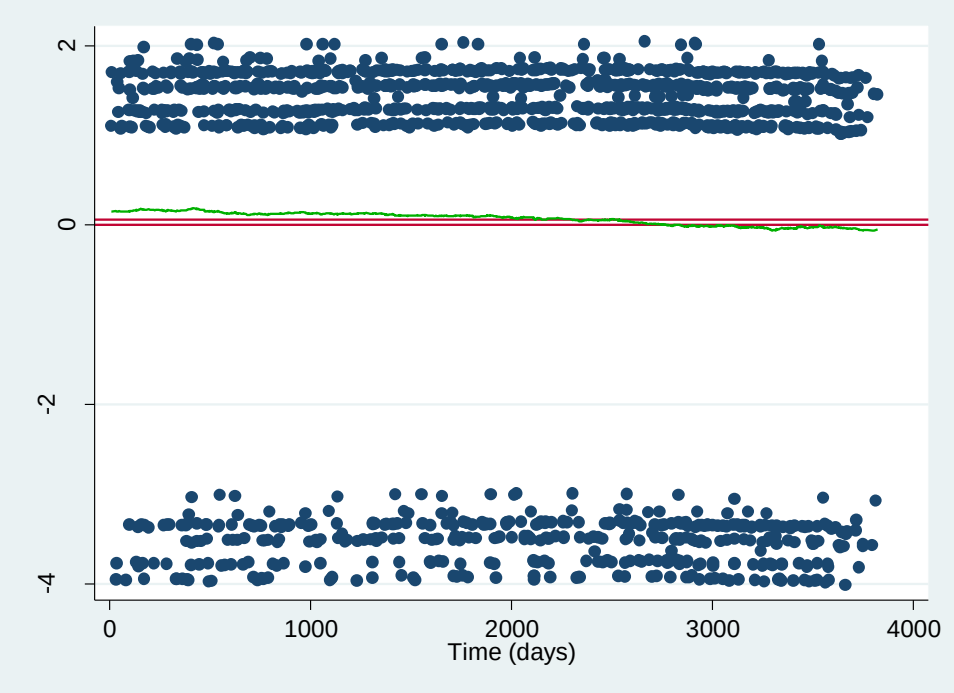
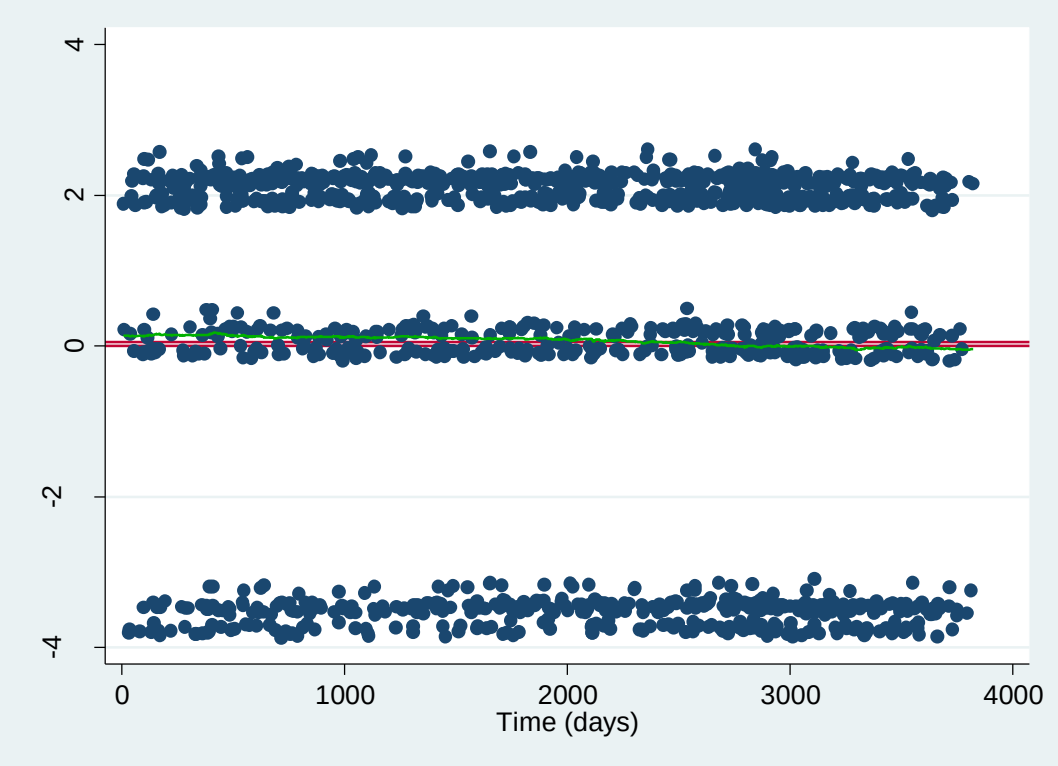


Table AV.4. Results of Schoenfeld tests for baseline complete case sample according to pain phenotype (ACR criteria) (n=10953)			
	Chi2	**df**	**p**
Pain but not ACR WP	2.64	1	0.1039
ACR WP	2.10	1	0.1471
Age	2.62	1	0.1056
Sex	1.29	1	0.2570
Education	1.87	1	0.1716
Adequacy of income	0.35	1	0.5557
Global test	9.66	6	0.1399
df=degrees of freedom			

Figure AV.4 a-b. Plot of Schoenfeld residuals for baseline complete case sample (n=10953) according pain phenotype (ACR criteria)

a) Pain but not ACR WP



b) ACR WP

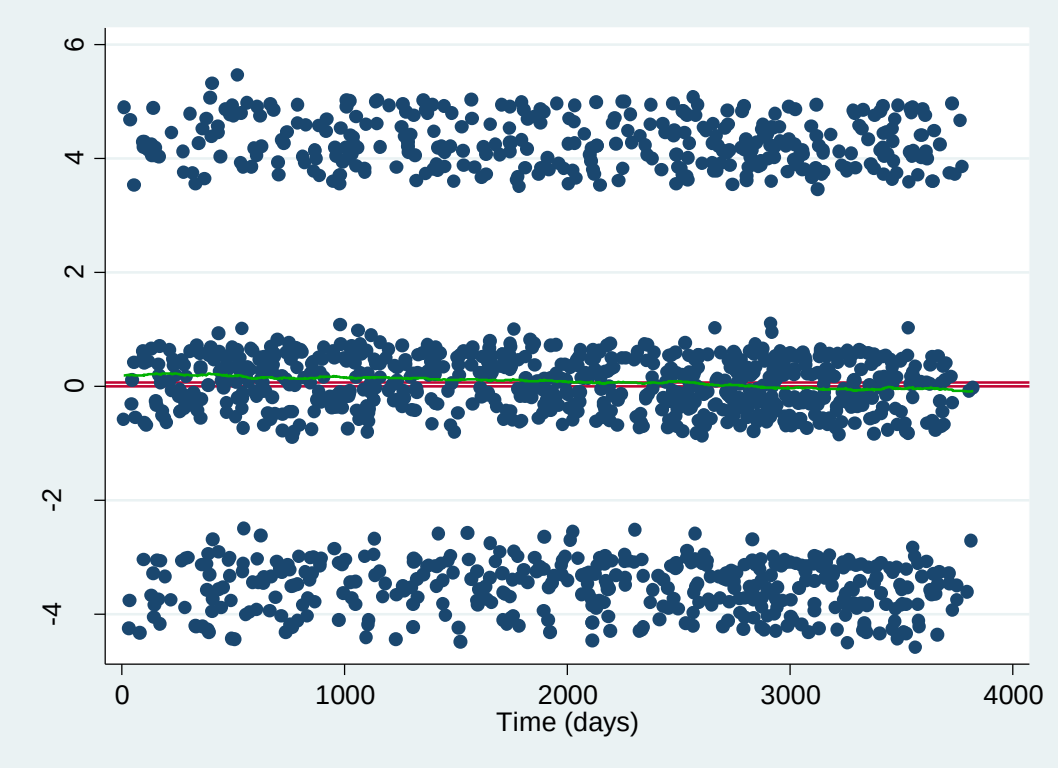
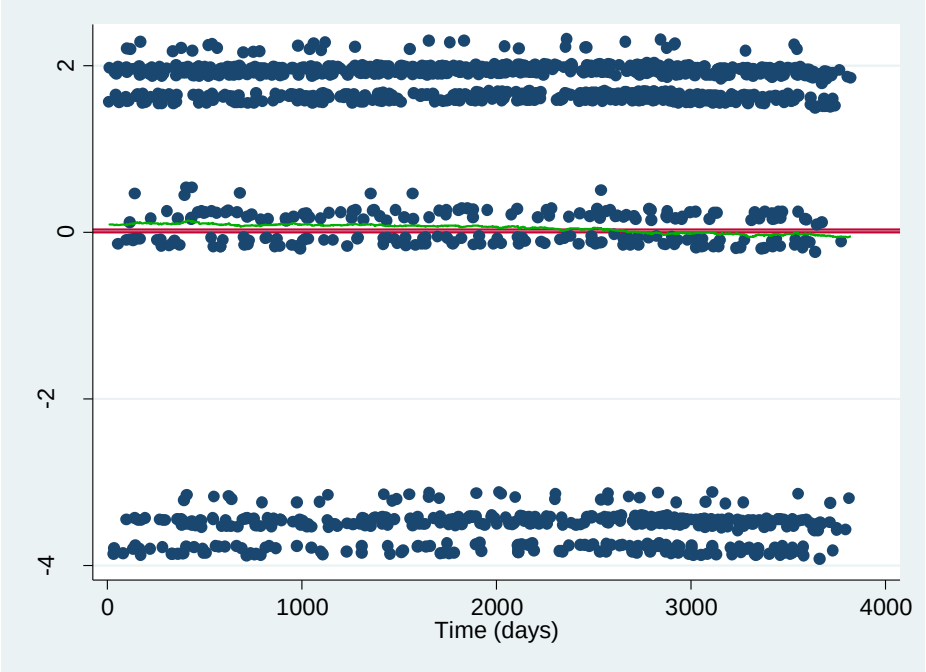


Table AV.5. Results of Schoenfeld tests for baseline complete case sample according to pain phenotype (Manchester criteria) (n=10953)			
	Chi2	**df**	**p**
Pain but not Manchester WP	1.60	1	0.2056
Manchester WP	5.95	1	0.0147
Age	2.38	1	0.1231
Sex	1.63	1	0.2021
Education	1.91	1	0.1675
Adequacy of income	0.53	1	0.4650
Global test	12.44	6	0.0528
df=degrees of freedom			

Figure AV.5 a-b. Plot of Schoenfeld residuals for baseline complete case sample (n=10953) according to pain phenotype (Manchester criteria)

a) Pain but not Manchester WP



b) Manchester WP

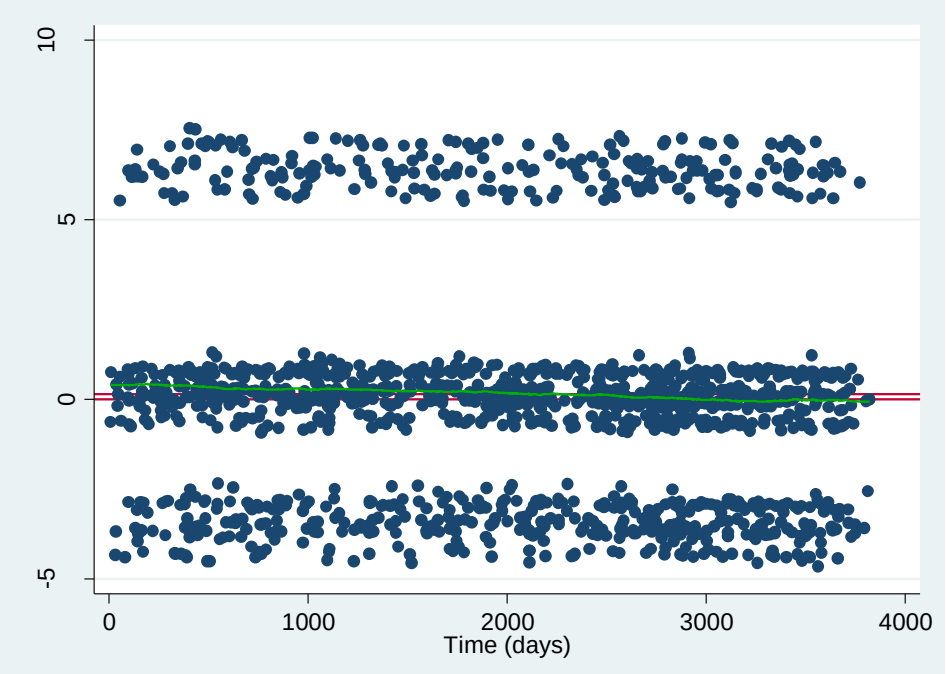
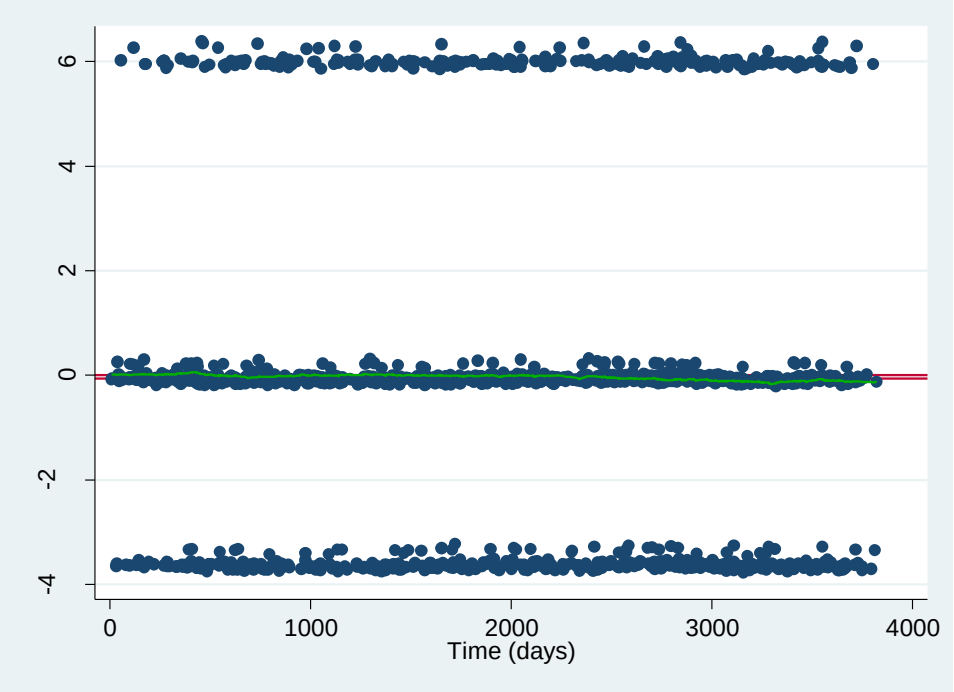


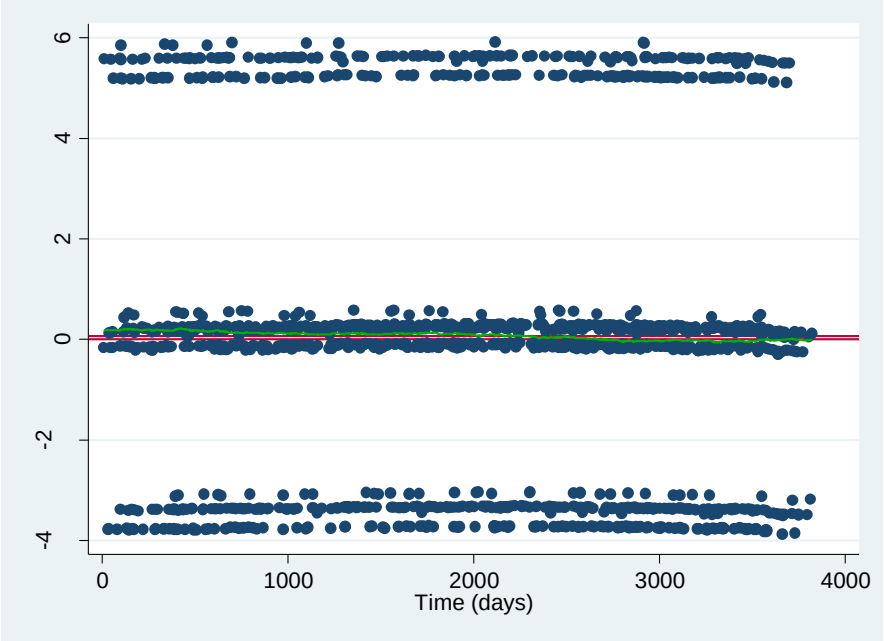
Table AV.6. Results of Schoenfeld tests for baseline complete case sample according to number of pain sites (n=10953)			
	Chi2	**df**	**p**
1-3 sites	0.49	1	0.4843
4-6 sites	3.30	1	0.0694
7-11 sites	0.11	1	0.7407
12+ sites	4.88	1	0.0271
Age	2.68	1	0.1014
Sex	1.37	1	0.2417
Education	1.78	1	0.1826
Adequacy of income	0.50	1	0.4777
Global test	13.29	8	0.1022
df=degrees of freedom			

Figure AV.6 a-d. Plot of Schoenfeld residuals for baseline complete case sample (n=10953) according number of pain sites

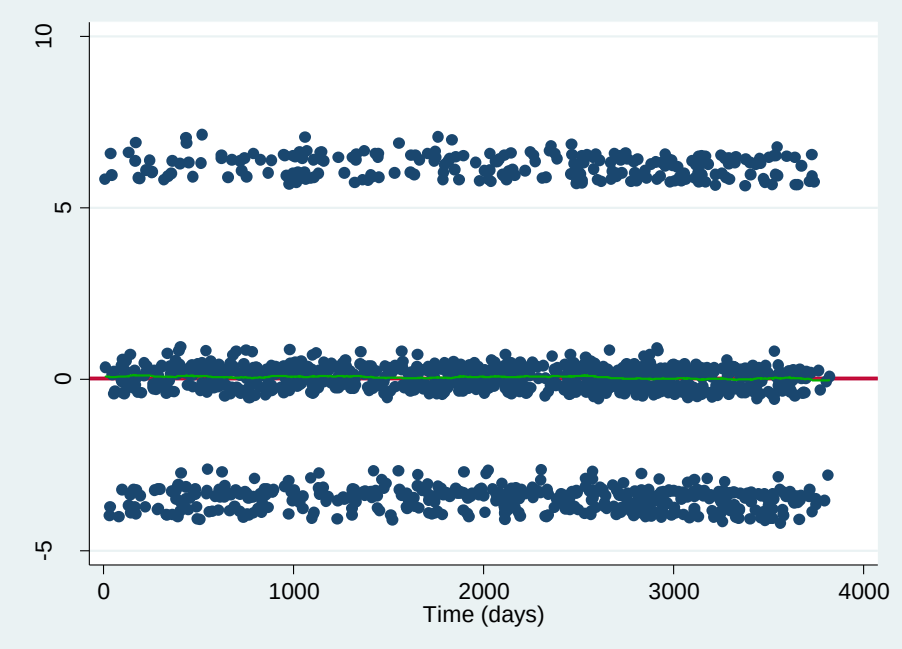
a) 1-3 sites



b) 4-6 sites



c) 7-11 sites



d) 12+ sites

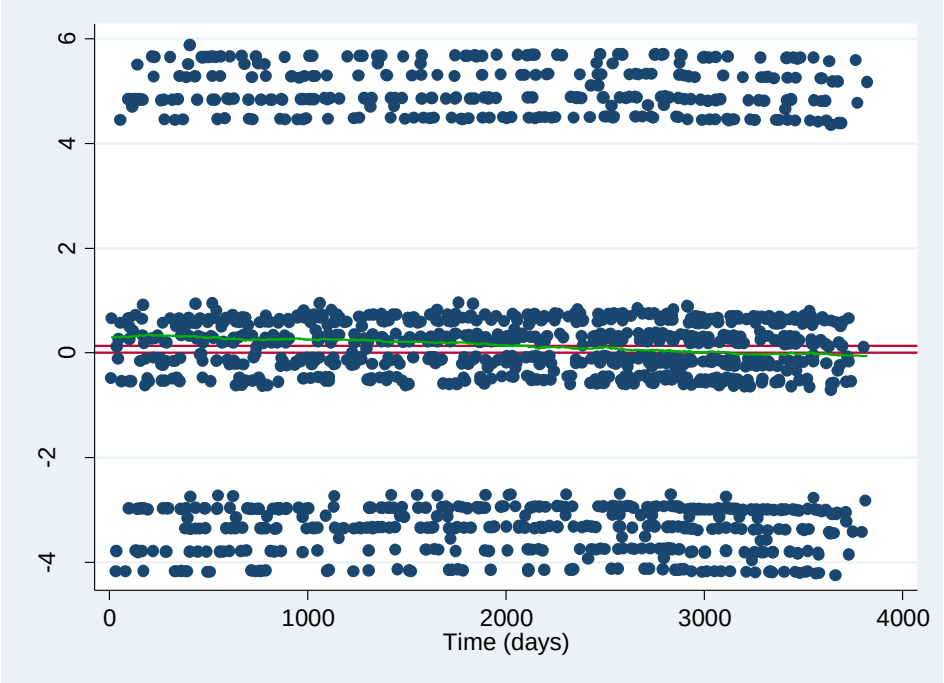
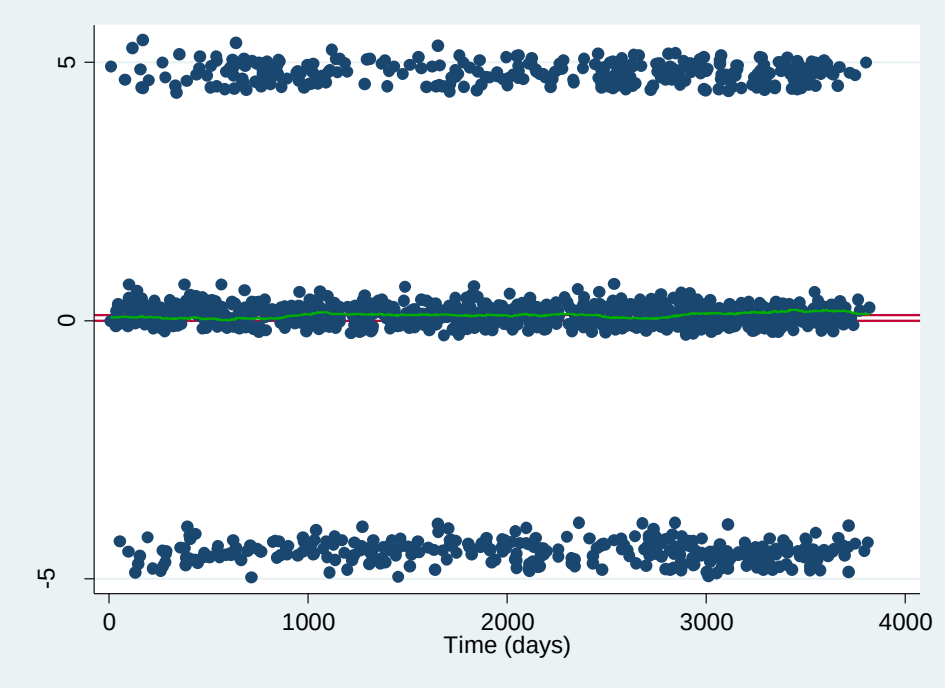


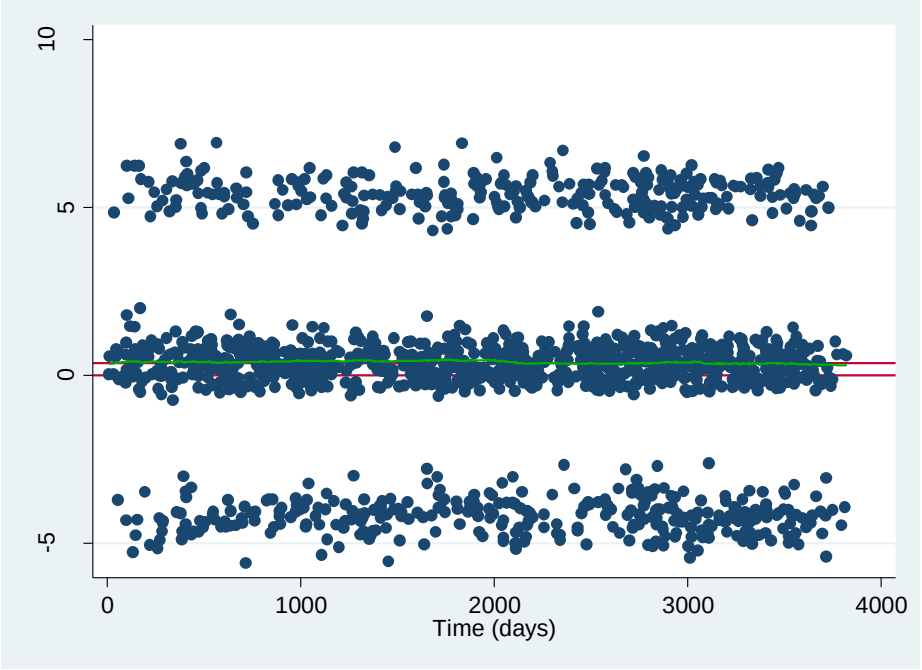
Table AV.7. Results of Schoenfeld tests for baseline complete case sample according to pain interference (n=10985)			
	Chi2	**df**	**p**
A little	0.15	1	0.7001
Moderately	1.07	1	0.3001
Quite a bit	2.74	1	0.0977
Extremely	11.22	1	0.0008
Age	4.75	1	0.0292
Sex	2.32	1	0.1273
Education	1.96	1	0.1617
Adequacy of income	1.41	1	0.2353
Global test	21.43	8	0.0061
df=degrees of freedom			

Figure AV.7 a-d. Plot of Schoenfeld residuals for baseline complete case sample (n=10985) according to pain interference

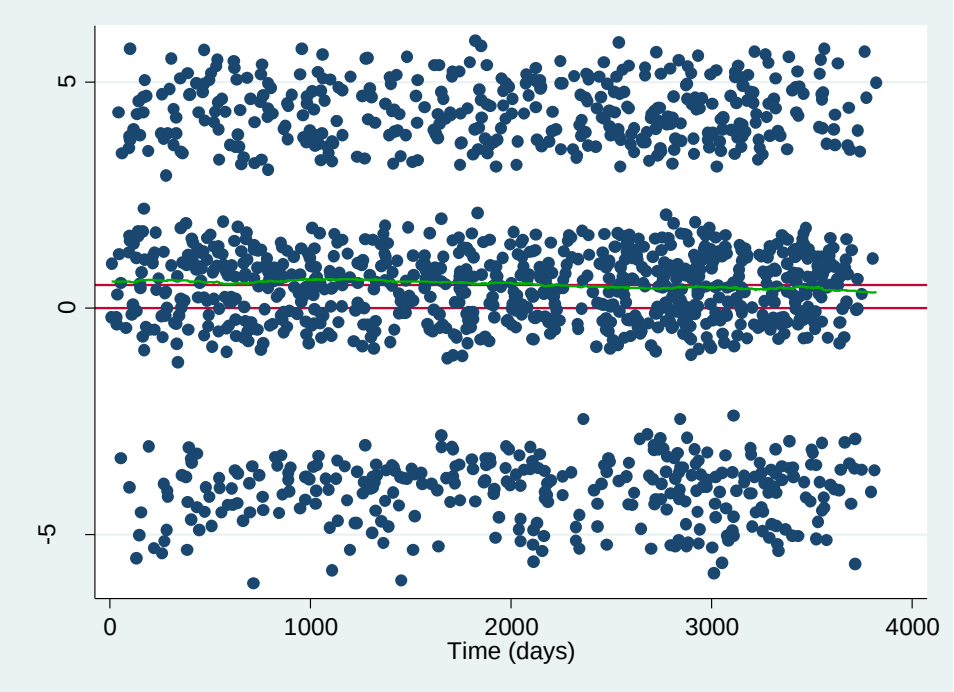
a) A little



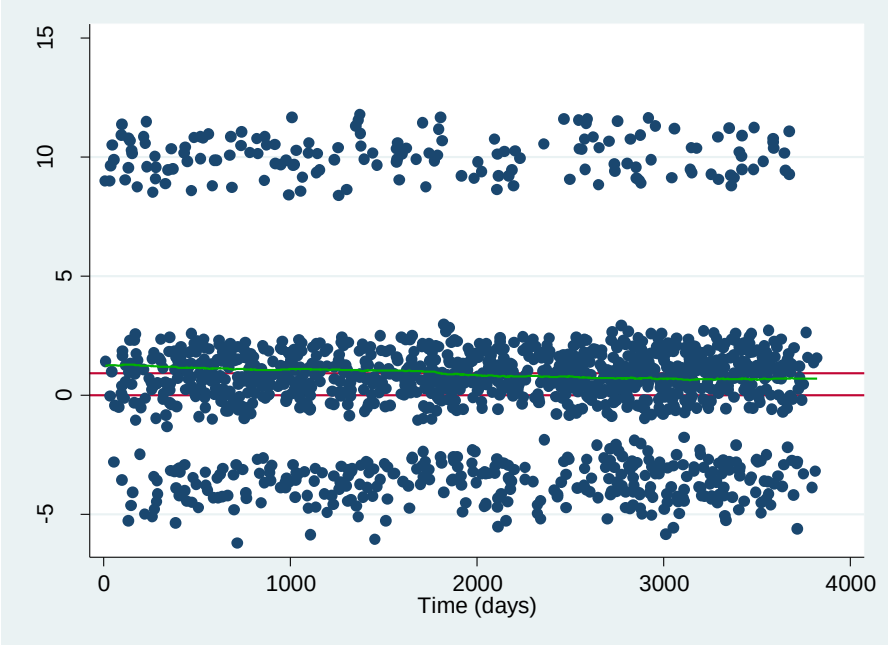
b) Moderately



c) Quite a bit



d) Extremely



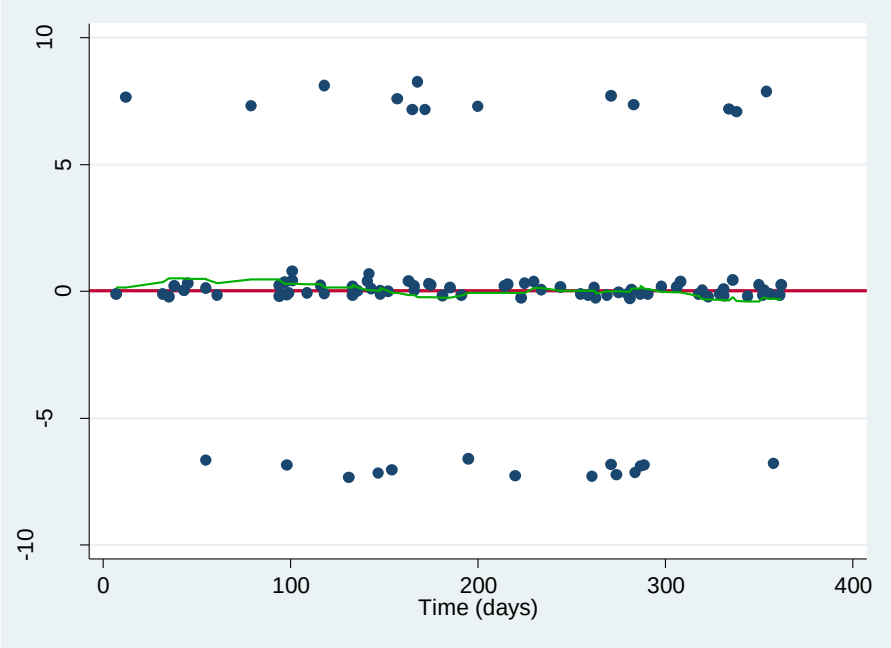
PAIN INTERFERENCE - TIMEBANDS

Table AV. 8. Results of Schoenfeld tests for the complete case sample according to pain interference 0-365 days (n=10985)			
	Chi2	**df**	**p**
A little	0.18	1	0.6672
Moderately	1.37	1	0.2424
Quite a bit	0.01	1	0.9373
Extremely	1.24	1	0.2659
Age	3.64	1	0.0566
Sex	0.01	1	0.9085
Education	2.31	1	0.1286
Adequacy of income	0.00	1	0.9520
Global test	10.88	8	0.2088
df=degrees of freedom			

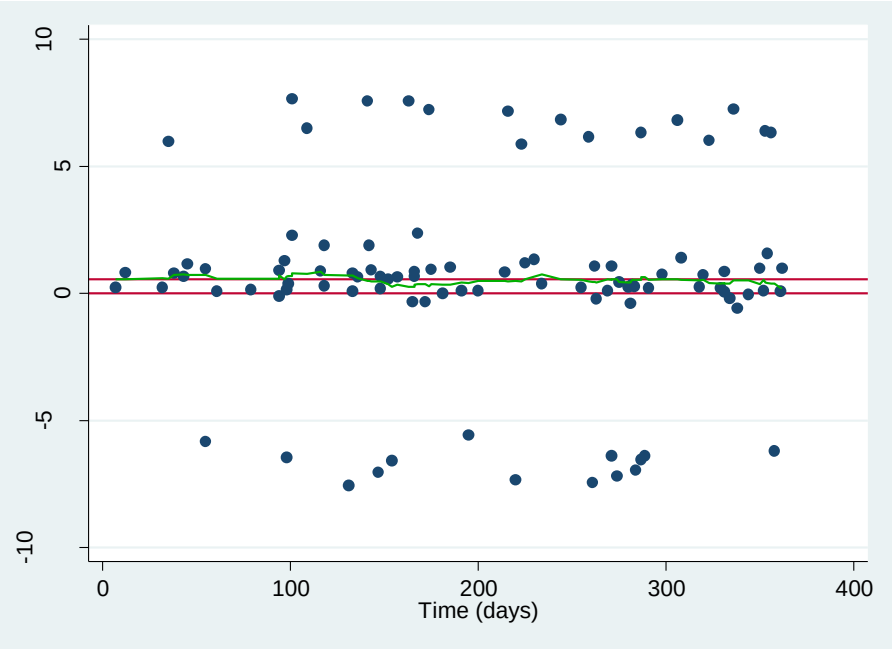
TIMEBAND 1

Figure AV.8 a-d. Plot of Schoenfeld residuals for baseline complete case sample (n=10985) according to pain interference (0-365 days)

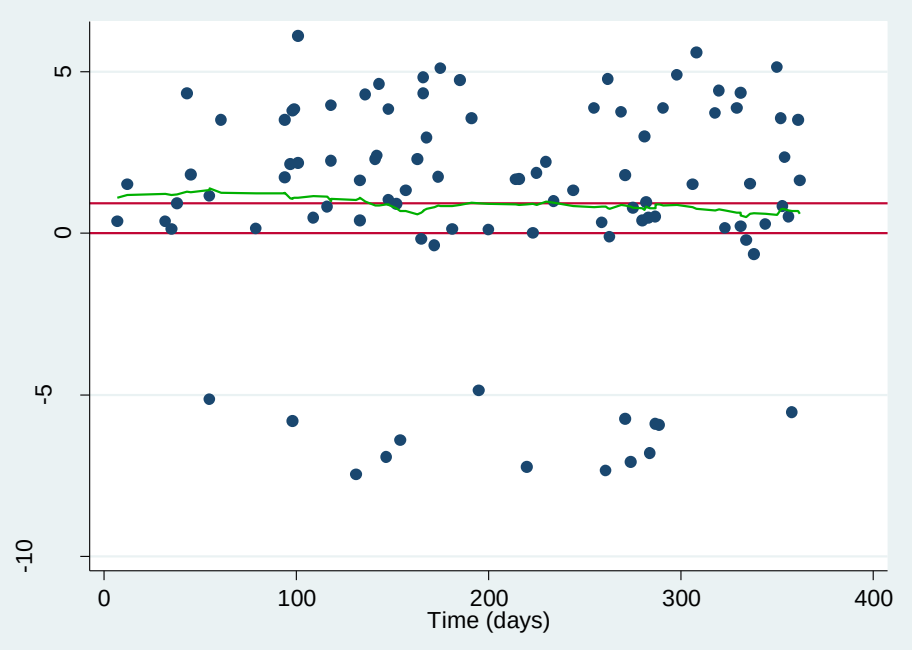
a) A little



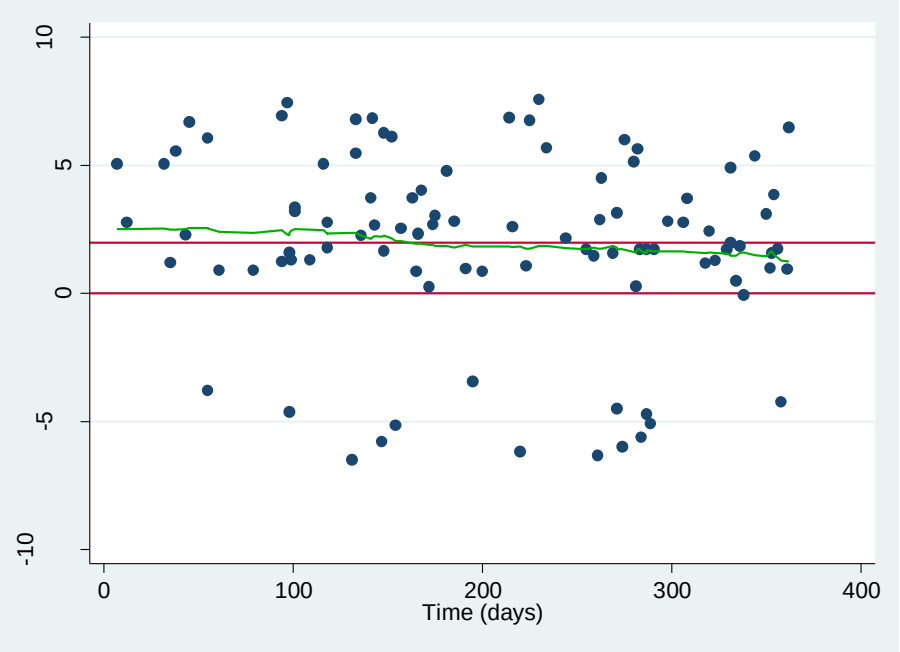
b) Moderately



c) Quite a bit



d) Extremely

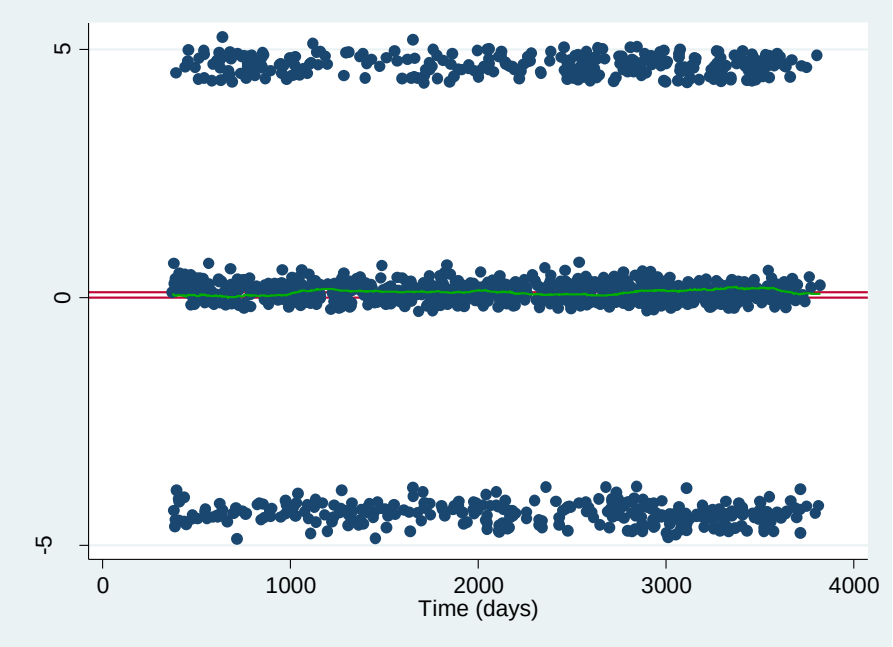


TIMEBAND 2

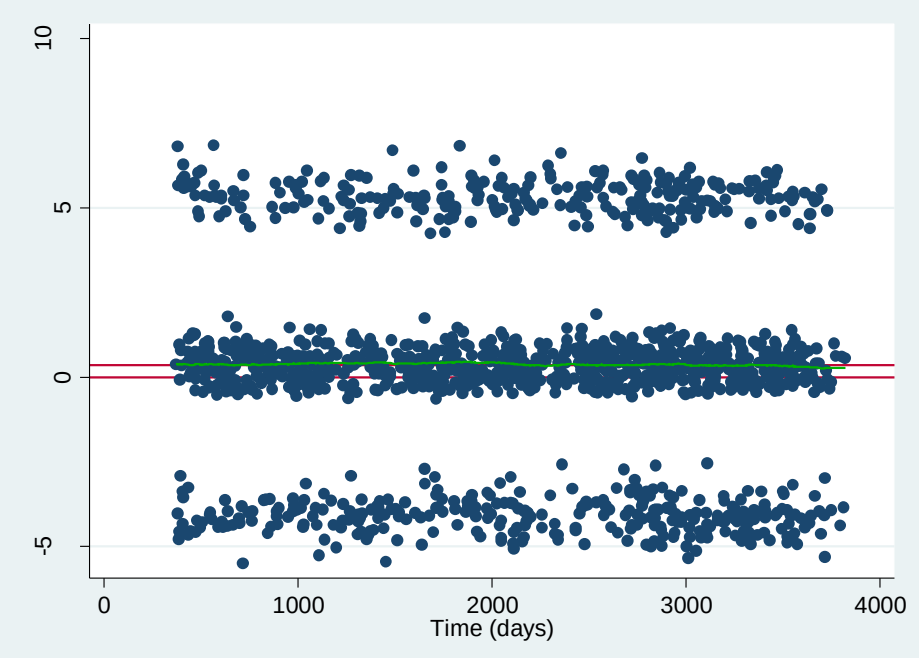
Table AV.9. Results of Schoenfeld tests for the complete case sample according to pain interference 365+ days (n=10888)			
	Chi2	**df**	**p**
A little	0.01	1	0.9413
Moderately	1.16	1	0.2813
Quite a bit	2.85	1	0.0914
Extremely	3.98	1	0.0460
Age	1.46	1	0.2273
Sex	0.88	1	0.3484
Education	2.57	1	0.1090
Adequacy of income	6.59	1	0.0102
Global test	14.87	8	0.0617
df=degrees of freedom			

Figure AV.9 a-d. Plot of Schoenfeld residuals for baseline complete case sample (n=10888) according to pain interference (365days+)

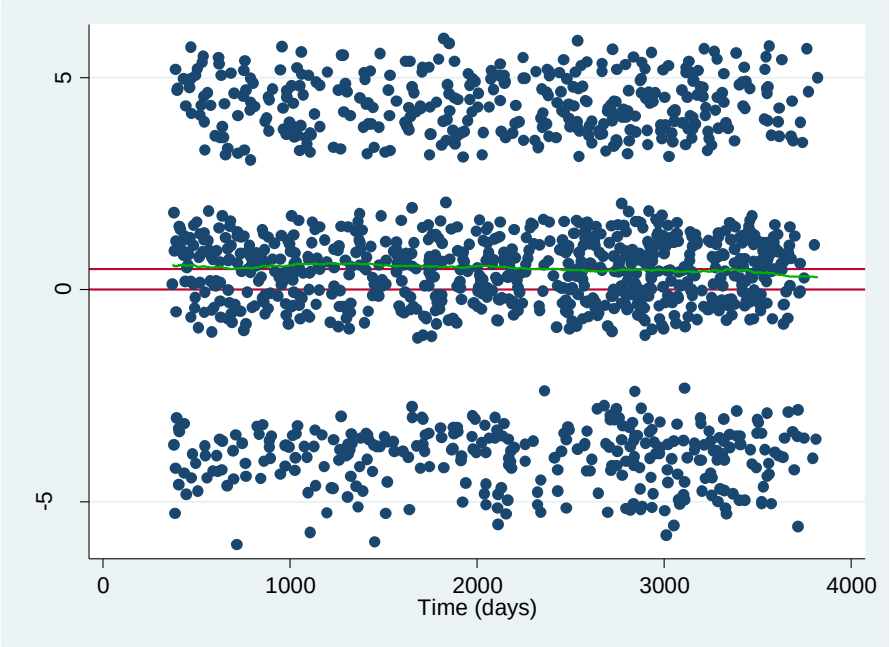
a) A little



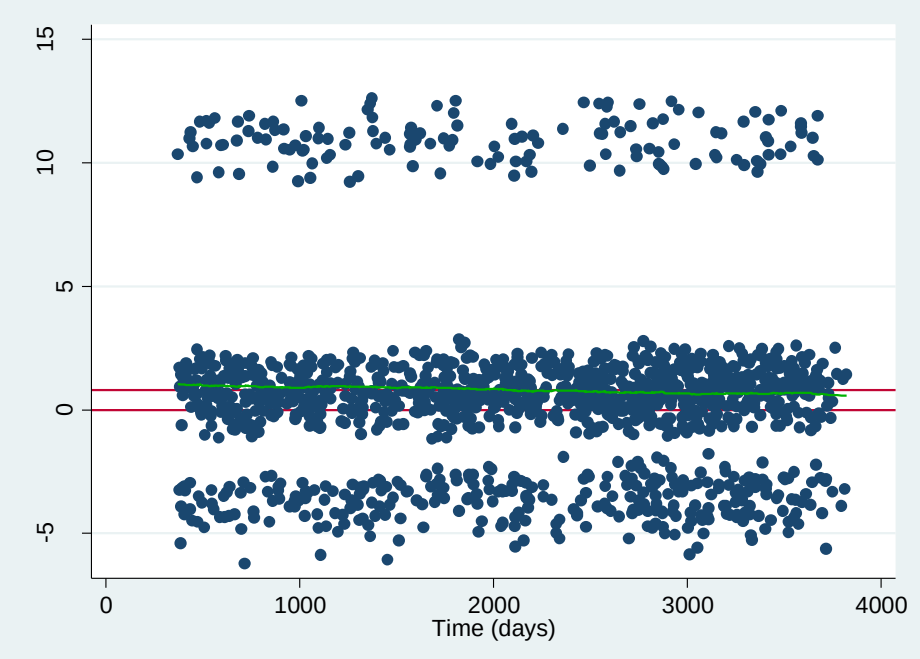
b) Moderately



c) Quite a bit



d) Extremely



Cause specific mortality (ELSA only)

Table AV.10 Results of Schoenfeld tests for complete case sample for cancer deaths for those often troubled with pain (n=6324)			
	Chi2	**df**	**p**
Often troubled with pain	2.73	1	0.0982
Age	0.04	1	0.8409
Sex	0.28	1	0.5971
Education	0.03	1	0.8517
Wealth	1.12	1	0.2899
Global test	4.18	5	0.5232
df=degrees of freedom			

Figure AV.10. Plot of Schoenfeld residuals for cancer mortality for the complete case sample (n=6324) comparing those often troubled with pain to those not often troubled

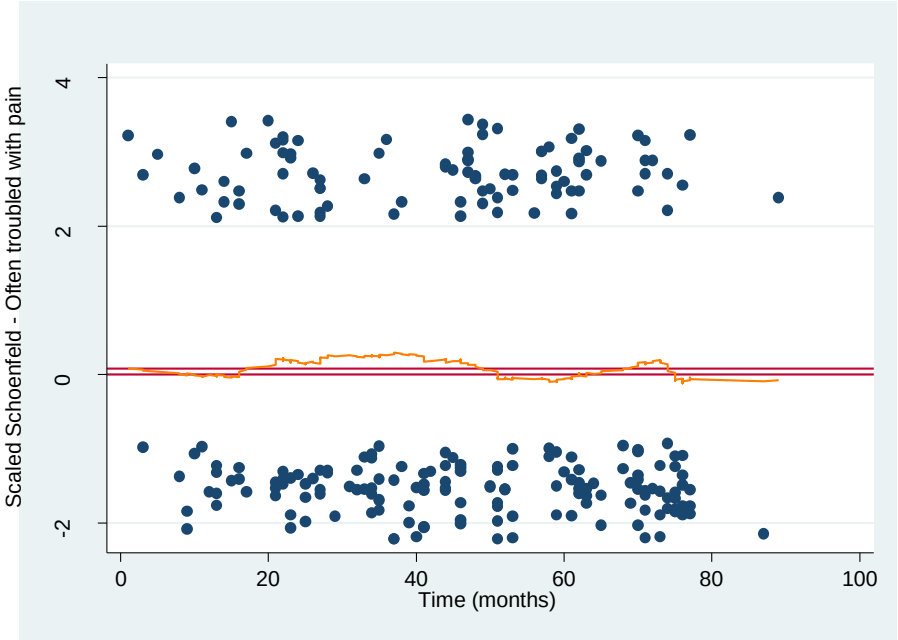
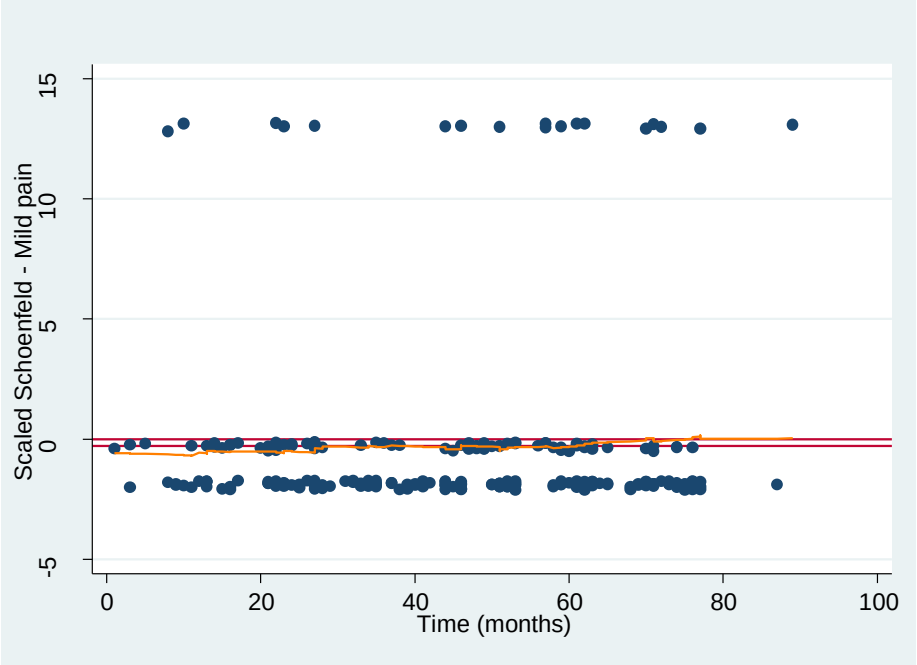


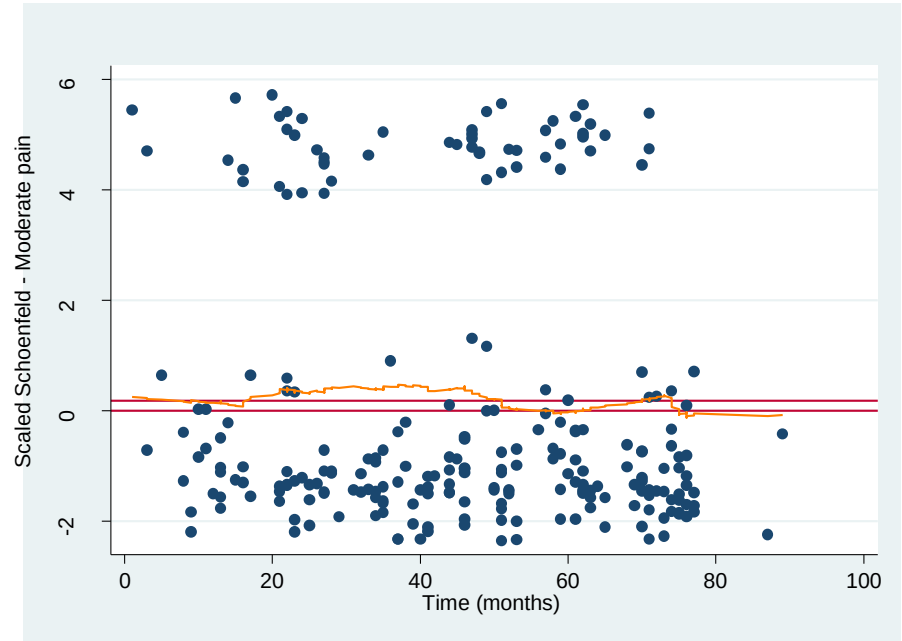
Table AV.11. Results of Schoenfeld tests for baseline sample for cancer deaths according to severity of pain (n=6324)			
	Chi2	**df**	**p**
Mild pain	0.31	1	0.5794
Moderate pain	4.06	1	0.0440
Severe pain	1.63	1	0.2016
Age	0.04	1	0.8346
Sex	0.34	1	0.5584
Education	0.09	1	0.7631
Wealth	1.49	1	0.2225
Global test	7.22	7	0.4062
df=degrees of freedom			

Figures AV.11.a-c. Plots of Schoenfeld residuals for cancer mortality for the complete case sample (n=6324) according to severity of pain

a) Mild pain



b) Moderate pain



c) Severe pain

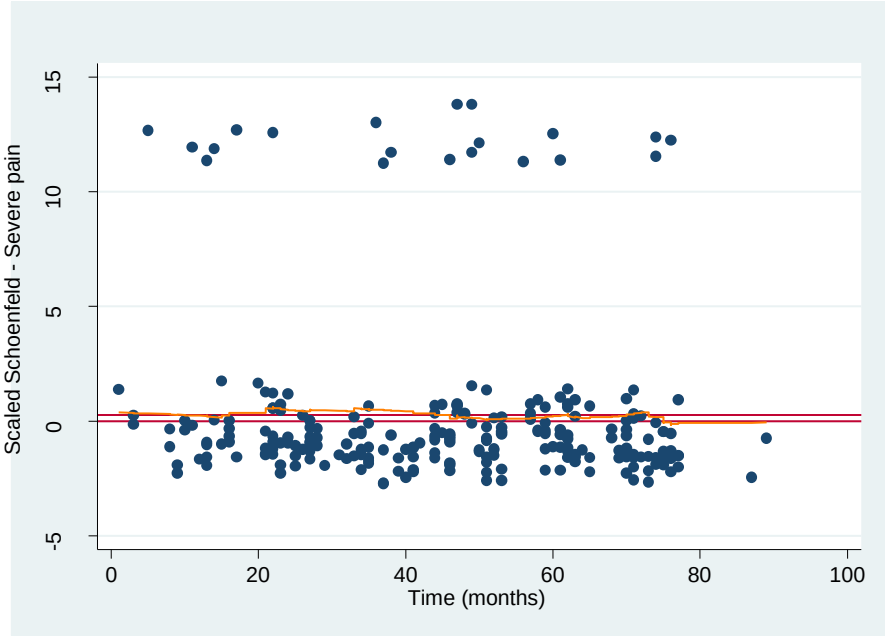


Table AV.12. Results of Schoenfeld tests for complete case sample for cardiovascular disease deaths for those often troubled with pain (n=6324)			
	Chi2	**df**	**P**
Often troubled with pain	0.33	1	0.5662
Age	0.08	1	0.7840
Sex	0.04	1	0.8461
Education	2.22	1	0.1366
Wealth	1.36	1	0.2431
Global test	3.32	5	0.6507
df=degrees of freedom			

Figure AV.12. Plot of Schoenfeld residuals for cardiovascular disease mortality for the complete case sample (n=6324) comparing those often troubled with pain to those not often troubled

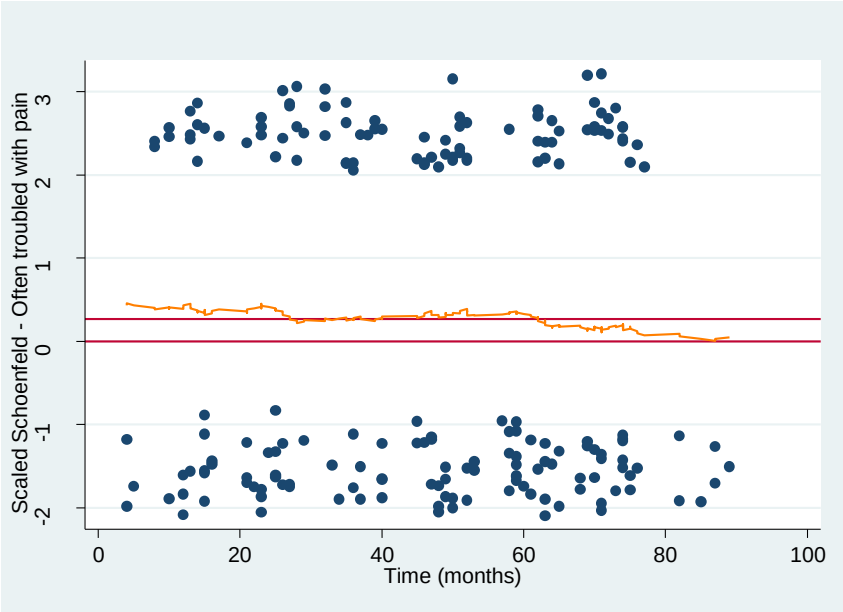
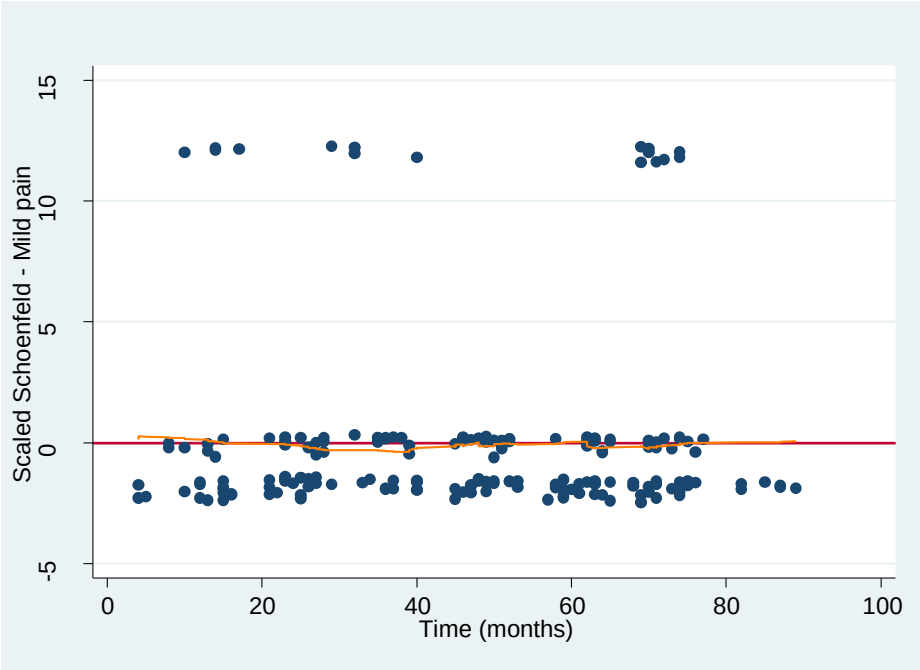


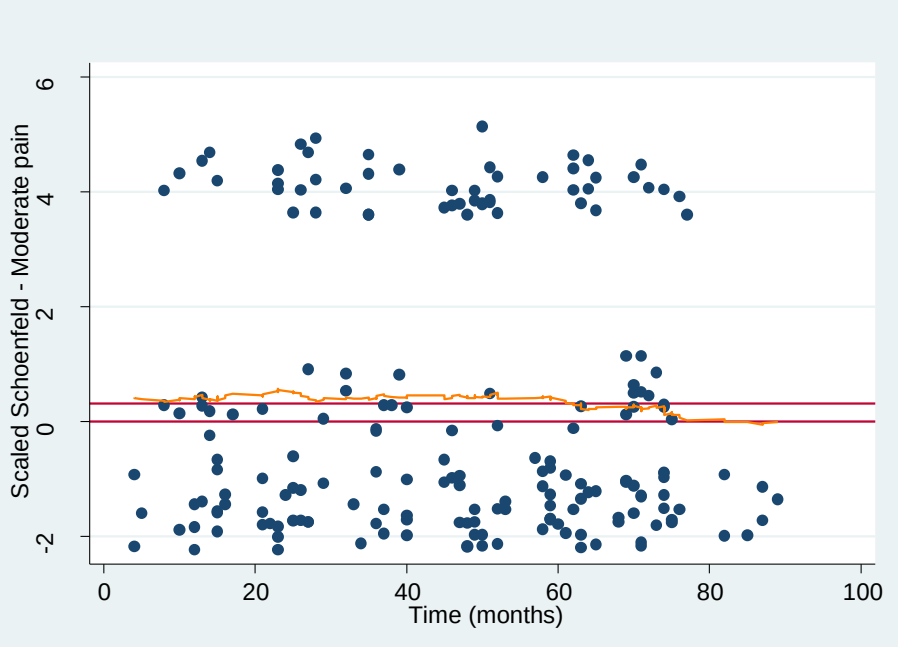
Table AV.13. Results of Schoenfeld tests for baseline sample for cardiovascular disease deaths according to severity of pain (n=6324)			
	Chi2	**df**	**p**
Mild pain	0.00	1	0.9829
Moderate pain	0.40	1	0.5285
Severe pain	0.16	1	0.6935
Age	0.06	1	0.8071
Sex	0.05	1	0.8306
Education	2.30	1	0.1291
Wealth	1.28	1	0.2586
Global test	3.48	7	0.8368
df=degrees of freedom			

Figures AV.13 a-c. Plots of Schoenfeld residuals for cardiovascular disease mortality for the complete case sample (n=6324) according to severity of pain

a) Mild pain



b) Moderate pain



Severe pain

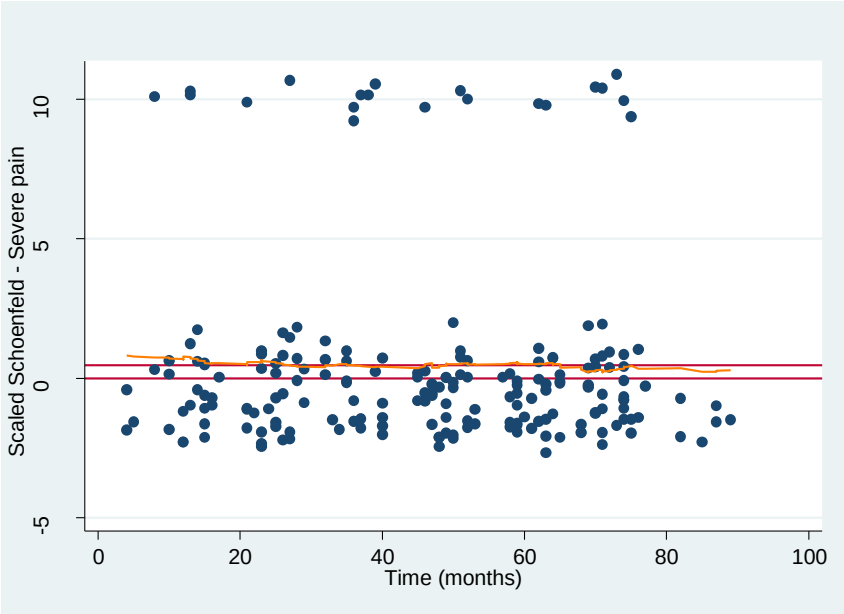


Table AV.14. Results of Schoenfeld tests for complete case sample for respiratory disease deaths for those often troubled with pain (n=6324)			
	Chi2	**df**	**p**
Often troubled with pain	5.51	1	0.0189
Age	2.57	1	0.1086
Sex	0.23	1	0.6293
Education	0.10	1	0.7558
Wealth	0.15	1	0.6952
Global test	9.07	5	0.1063
df=degrees of freedom			

Figure AV.14. Plot of Schoenfeld residuals for respiratory disease mortality for the complete case sample (n=6324) comparing those often troubled with pain to those not often troubled

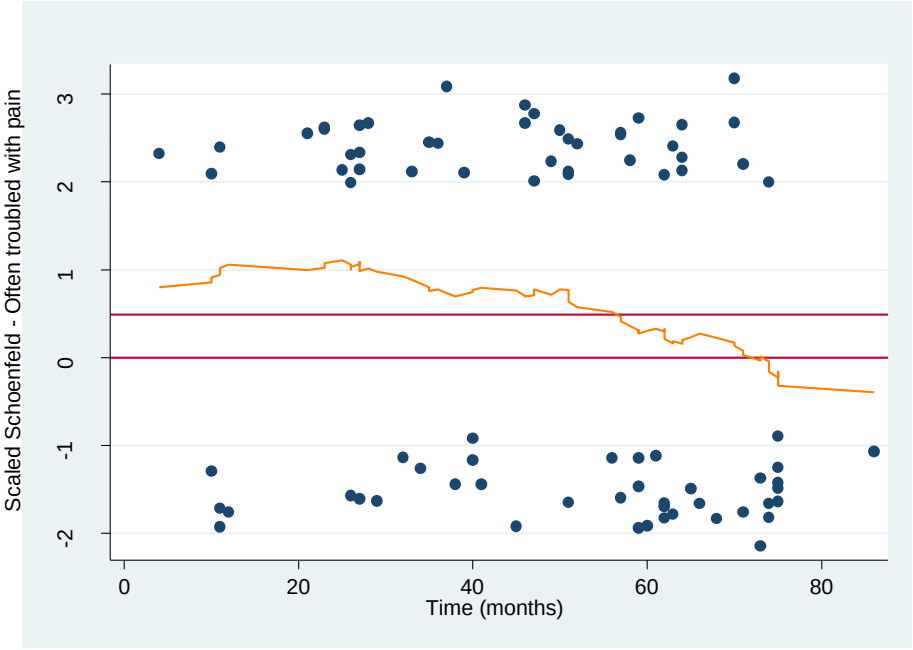
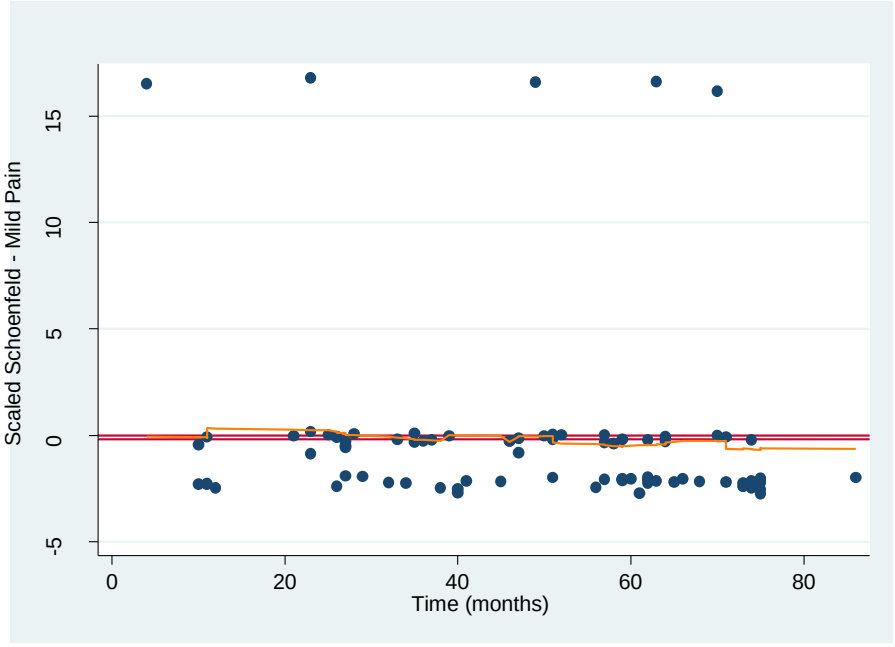


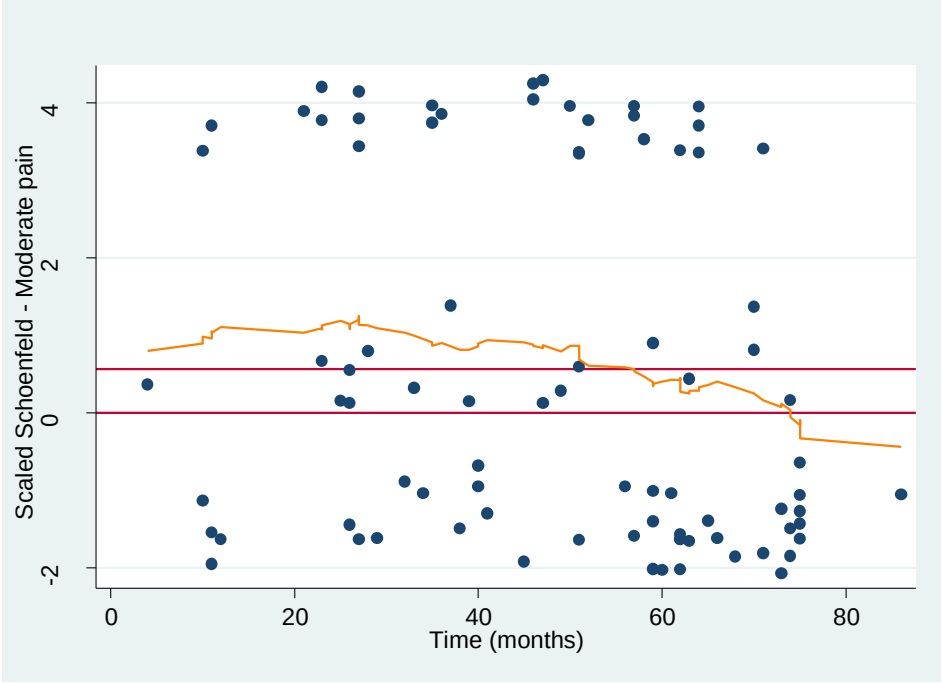
Table AV.15. Results of Schoenfeld tests for baseline sample for respiratory disease deaths according to severity of pain (n=6324)			
	Chi2	**df**	**p**
Mild pain	1.43	1	0.2321
Moderate pain	4.25	1	0.0391
Severe pain	2.09	1	0.1480
Age	2.50	1	0.1141
Sex	0.24	1	0.6277
Education	0.12	1	0.7299
Wealth	0.13	1	0.7178
Global test	9.02	7	0.2512
df=degrees of freedom			

Figures AV.15 a-c. Plots of Schoenfeld residuals for respiratory disease mortality for the complete case sample (n=6324) according to severity of pain

a) Mild pain



b) Moderate pain



c) Severe pain

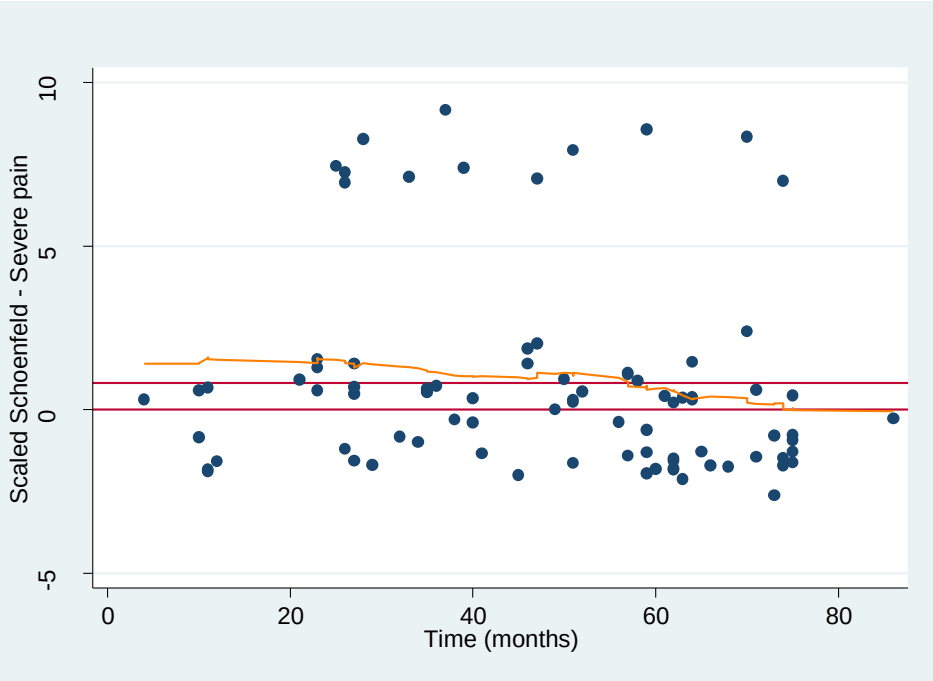


Table AV.16. Results of Schoenfeld tests for complete case sample for other (known) deaths for those often troubled with pain (n=6324)			
	Chi2	**df**	**p**
Often troubled with pain	2.09	1	0.1486
Age	1.35	1	0.2458
Sex	2.71	1	0.1000
Education	0.24	1	0.6208
Wealth	0.47	1	0.4942
Global test	6.76	5	0.2392
df=degrees of freedom			

Figure AV.16. Plot of Schoenfeld residuals for other (known) mortality for the complete case sample (n=6324) comparing those often troubled with pain to those not often troubled

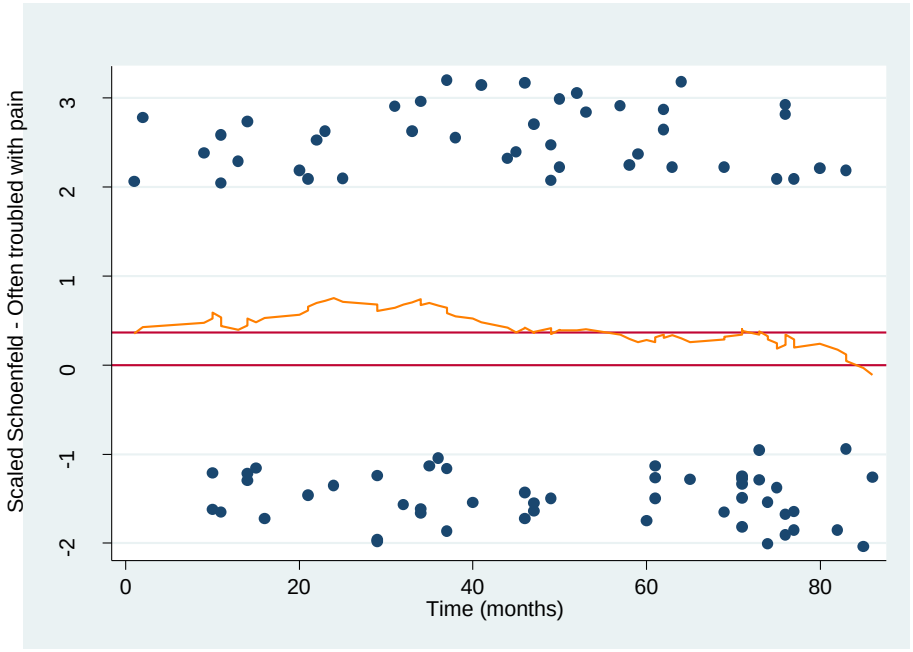
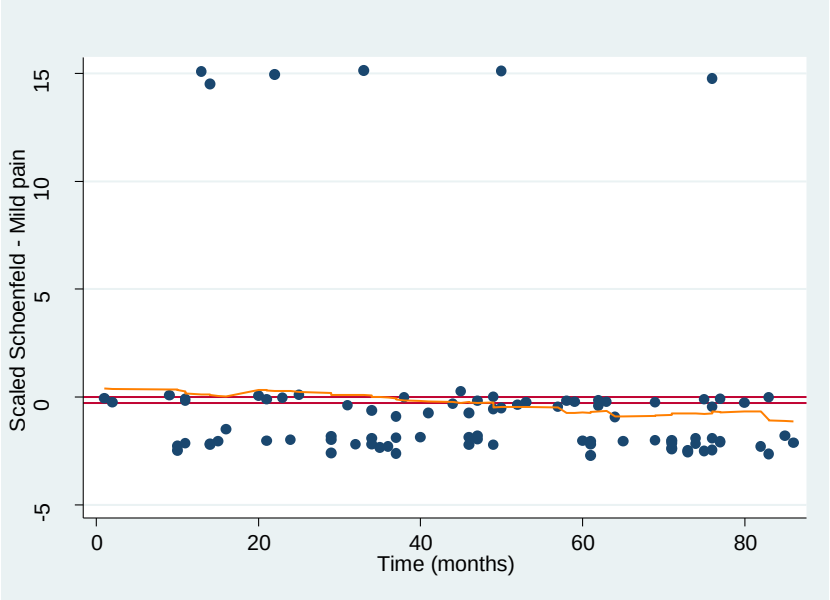


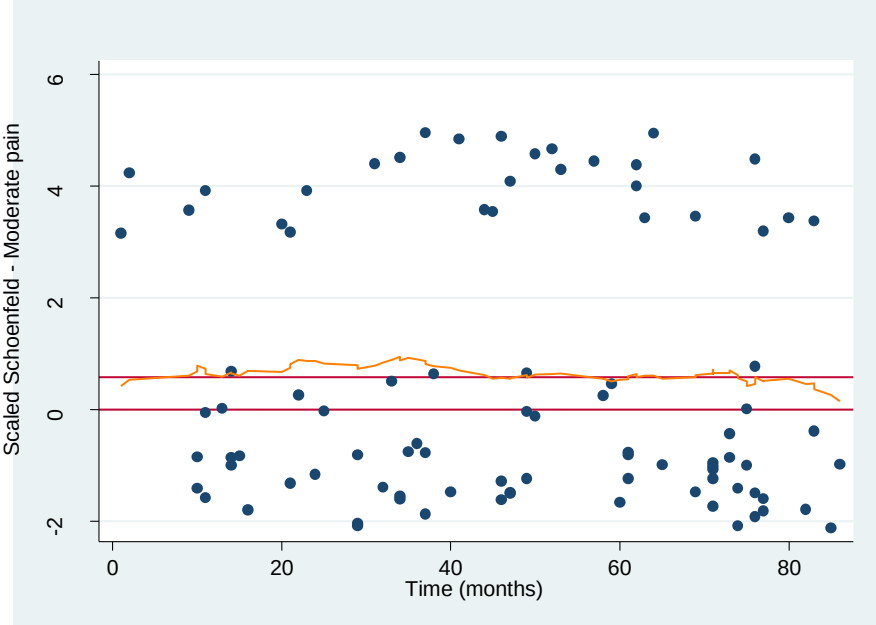
Table AV.17. Results of Schoenfeld tests for baseline sample for other deaths according to severity of pain (n=6324)			
	Chi2	**df**	**p**
Mild pain	2.82	1	0.0933
Moderate pain	0.89	1	0.3448
Severe pain	0.25	1	0.6145
Age	1.45	1	0.2287
Sex	2.48	1	0.1154
Education	0.32	1	0.5687
Wealth	0.62	1	0.4297
Global test	7.96	7	0.3359
df=degrees of freedom			

Figures AV.17 a-c. Plots of Schoenfeld residuals for other (known) mortality for the complete case sample (n=6324) according to severity of pain

a) Mild pain



b) Moderate pain



c) Severe pain

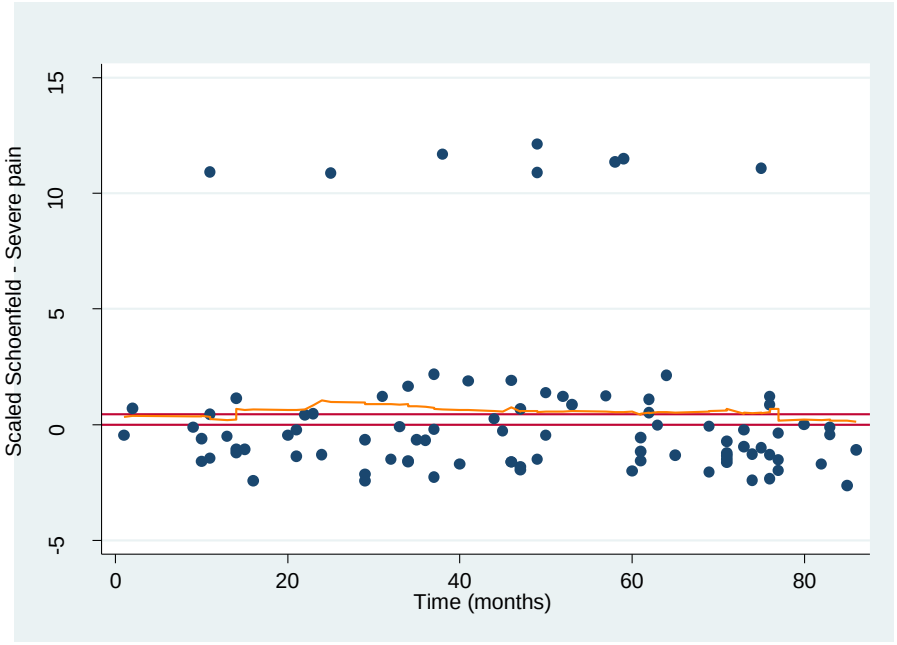


Table AV.18. Results of Schoenfeld tests for complete case sample for other (known) deaths for those often troubled with pain (n=6324)			
	Chi2	**df**	**p**
Often troubled with pain	0.02	1	0.8828
Age	1.67	1	0.1958
Sex	1.10	1	0.2953
Education	0.05	1	0.8154
Wealth	0.42	1	0.5174
Global test	4.76	5	0.4455
df=degrees of freedom			

Figure AV.18. Plot of Schoenfeld residuals for unknown mortality for the complete case sample (n=6324) comparing those often troubled with pain to those not often troubled

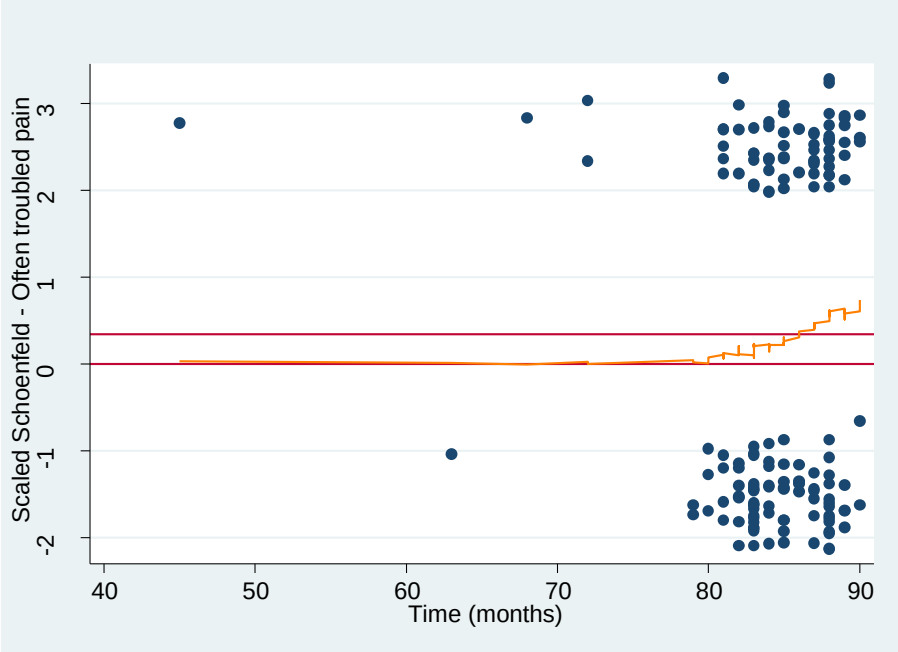
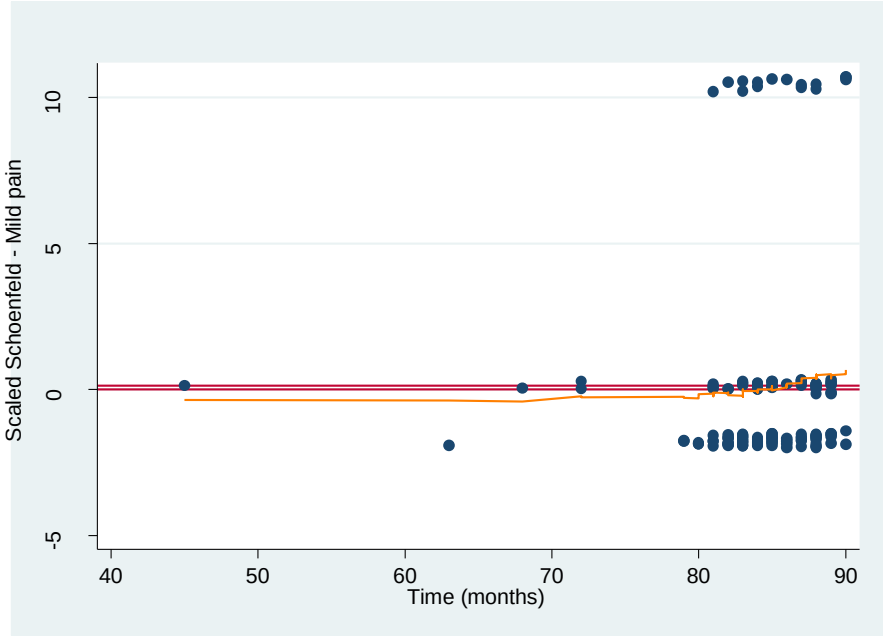


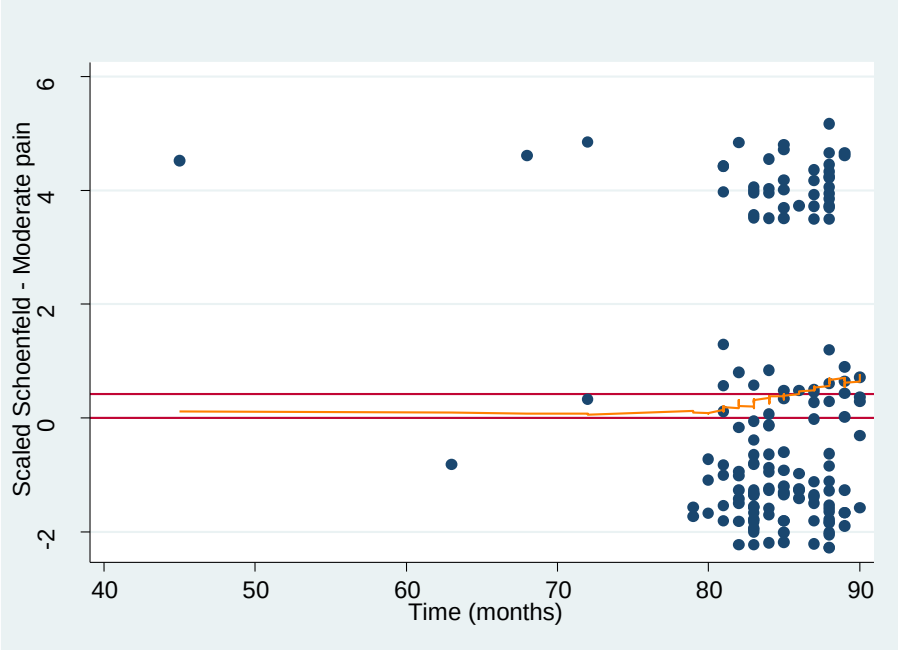
Table AV.19. Results of Schoenfeld tests for baseline sample for other deaths according to severity of pain (n=6324)			
	Chi2	**df**	**p**
Mild pain	1.24	1	0.2654
Moderate pain	0.67	1	0.4126
Severe pain	0.02	1	0.8998
Age	1.64	1	0.2004
Sex	1.24	1	0.2654
Education	0.10	1	0.7531
Wealth	0.60	1	0.4385
Global test	7.17	7	0.4109
df=degrees of freedom			

Figures AV.19 a-c. Plots of Schoenfeld residuals for unknown mortality for the complete case sample (n=6324) according to severity of pain

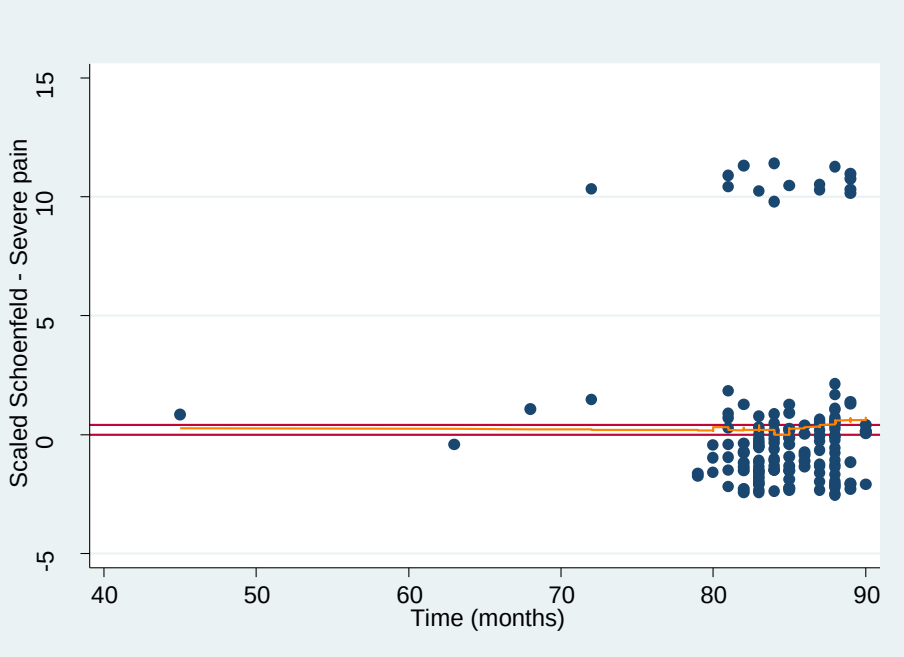
a) Mild pain



b) Moderate pain



c) Severe pain



Appendix VI - Survival models with interaction terms

Table AVI.1 Interactions between pain phenotype and sex and pain phenotype and comorbidity in the ELSA complete case sample (n=6324)			
Pain phenotype	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
Not often troubled	Reference	Reference	Reference
Often troubled x sex	0.94 (0.71, 1.26)	0.89 (0.67, 1.19)	0.90 (0.67, 1.20)
Not often troubled	Reference	Reference	Reference
Mild x sex	1.11 (0.65, 1.90)	1.32 (0.77, 2.26)	1.31 (0.76, 2.26)
Moderate x sex	0.80 (0.57, 1.12)	0.72 (0.51, 1.00)	0.73 (0.52, 1.03)
Severe x sex	1.16 (0.71, 1.89)	0.92 (0.56, 1.50)	0.94 (0.58, 1.55)
Not often troubled	Reference	Reference	Reference
Often troubled x comorbidity	**1.50 (1.03, 2.19)**	1.12 (0.77, 1.64)	1.10 (0.76, 1.61)
Not often troubled	Reference	Reference	Reference
Mild x comorbidity	1.53 (0.79, 2.96)	0.96 (0.49, 1.86)	0.97 (0.50, 1.89)
Moderate x comorbidity	1.23 (0.77, 1.98)	1.05 (0.65, 1.69)	1.02 (0.64, 1.64)
Severe x comorbidity	1.41 (0.63, 3.13)	1.21 (0.54, 2.69)	1.21 (0.54, 2.70)
MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval **Model 1: Crude** **Model 2:Adjusted for age, sex** **Model 3: Adjusted for age, sex, education, wealth**			

Table AVI.2 Interactions between pain phenotype and sex in the NorStOP complete case sample (n=10985)			
Pain phenotype	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
No pain	Reference	Reference	Reference
Any pain x sex	0.98 (0.78, 1.23)	0.92 (0.74, 1.16)	0.93 (0.74, 1.17)
No pain	Reference	Reference	Reference
Pain but not ACR x sex	1.03 (0.81, 1.31)	0.97 (0.76, 1.24)	0.98 (0.77, 1.25)
ACR WP x sex	0.91 (0.68, 1.21)	0.83 (0.63, 1.11)	0.84 (0.63, 1.11)
No pain	Reference	Reference	Reference
Pain but not Manchester WP x sex	1.02 (0.81, 1.30)	0.98 (0.77, 1.24)	0.98 (0.77, 1.25)
Manchester WP x sex	0.84 (0.61, 1.15)	0.74 (0.54, 1.02)	0.75 (0.54, 1.03)
No sites	Reference	Reference	Reference
1-3 sites x sex	1.10 (0.80, 1.51)	0.96 (0.70, 1.32)	0.96 (0.70, 1.33)
4-6 sites x sex	1.01 (0.74, 1.37)	0.97 (0.71, 1.32)	0.98 (0.72, 1.33)
7-11 sites x sex	0.99 (0.72, 1.37)	0.99 (0.72, 1.36)	0.99 (0.72, 1.36)
12+ sites x sex	0.84 (0.62, 1.13)	0.80 (0.59, 1.08)	0.81 (0.60, 1.09)
MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval **Model 1: Crude** **Model 2: Adjusted for age, sex** **Model 3: Adjusted for age, sex, education, wealth**			

Table AVI.3 Interactions between pain phenotype and comorbidity in the NorStOP complete case sample (n=10985)			
Pain phenotype	**Model 1 MRR (95% CI)**	**Model 2 MRR (95% CI)**	**Model 3 MRR (95% CI)**
No pain	Reference	Reference	Reference
Any pain x comorbidity	0.74 (0.49, 1.10)	0.73 (0.49, 1.09)	0.73 (0.49, 1.08)
No pain	Reference	Reference	Reference
Pain but not ACR x comorbidity	0.72 (0.48, 1.10)	0.68 (0.45, 1.04)	0.68 (0.45, 1.03)
ACR WP x comorbidity	0.86 (0.43, 1.72)	0.91 (0.46, 1.83)	0.90 (0.45, 1.81)
No pain	Reference	Reference	Reference
Pain but not Manchester WP x comorbidity	0.72 (0.48, 1.08)	0.69 (0.46, 1.03)	0.68 (0.46, 1.03)
Manchester WP x comorbidity	1.03 (0.32, 3.34)	1.14 (0.35, 3.71)	1.14 (0.35, 3.70)
No sites	Reference	Reference	Reference
1-3 sites x comorbidity	**0.59 (0.36, 0.97)**	**0.51 (0.31, 0.83)**	**0.51 (0.31, 0.83)**
4-6 sites x comorbidity	0.77 (0.44, 1.35)	0.76 (0.43, 1.33)	0.75 (0.43, 1.32)
7-11 sites x comorbidity	1.07 (0.48, 2.40)	1.16 (0.52, 2.59)	1.15 (0.51, 2.57)
12+ sites x comorbidity	0.82 (0.32, 2.07)	0.92 (0.36, 2.34)	0.91 (0.36, 2.31)
MRR=Mortality Rate Ratio, 95% CI = 95% confidence interval **Model 1: Crude** **Model 2: Adjusted for age, sex** **Model 3: Adjusted for age, sex, education, wealth**			

Appendix VII - Measurement of the proposed mediators in the ELSA and NorStOP datasets

Lifestyle factors

Physical activity

In ELSA, participants were asked to indicate whether they took part in vigorous, moderate or mild physical activities more than once a week, once a week, one to three times a month or hardly ever. Similar to previous research, (Hamer, Molloy, de Oliveira, & Demakakos, 2009) four physical activity categories were derived (none, mild activity, moderate and vigorous activity at least once a week). Three dichotomous variables were created for vigorous, moderate and mild activities scored as 1 if a participant indicated they took part in that level of activity once a week or more and 0 if not. A summary variable was then created whereby if participants scored 1 for vigorous activity more than once a week they were allocated to this category, if they indicated moderate activity and did not separately indicate vigorous activity they were allocated to the 'moderate' category. It they indicated mild activity at least once a week and did not also indicate moderate or vigorous activity they were allocated to the 'mild' activity category. If they did not indicate activity at any of the above levels at least once a week they were allocated to the 'no activity' category. This variable was then dichotomised for use in the mediation analysis to compare no/mild activity to moderate/vigorous activity at least once a week. No/mild activity has previously been used to form a category of low activity in ELSA (Hamer et al., 2009) and this formed the reference group for the analysis.

In NorStOP, two single items were used to measure the frequency of physical activity; frequency of going to activities outside the home and frequency of going for a walk for at

least ten to fifteen minutes. Participants were asked to indicate if they went out on all days, most days, some days, few days or no days. This was dichotomised into few/no days compared to all/most/some days. Frequency of going for a walk was categorised as daily, every other day, twice per week, less than twice per week, or not at all. This was dichotomised into less than weekly versus weekly or more. These dichotomies were chosen to be comparable to the physical activity variable from ELSA.

Smoking

In ELSA, smoking status was determined by asking participants to indicate whether they never smoked, used to be an occasional, regular or frequent smoker, or were a current smoker. The dichotomous variable used in the mediation analysis compared non-smokers (never and past) (reference) to current smokers.

In the NorStOP participants were asked to indicate their current smoking status and specify if they "never smoked", "previously smoked" or were "currently smoking". This variable was dichotomised into never/previous smokers (reference) versus current smokers.

The dichotomy of non-smoker/current smoker is a routinely used method of capturing smoker status, however the category of non-smoker will include ex-smokers and those who quit recently are at greater risk of disease than non-smokers (Marston et al., 2014). The earlier an individual stops smoking the greater the reduction mortality risk; in a study of 34,439 British doctors Doll et al. found stopping smoking at age 60, 50, 40 or 30 years of age meant a gain of 3,6,9 or 10 years of life expectancy respectively (Doll et al., 2004).

Alcohol consumption

In ELSA, participants were asked about the frequency of their alcohol consumption over the last 12 months. Responses options were 'not at all', ' once or twice a year', 'once every couple of months', 'once or twice a month', 'once or twice a week', three or four times a week', 'five or six days a week', and 'almost every day'. These options were categorised to alcohol consumption less than weekly (reference) and weekly or more often.

In the NorStOP sample, alcohol consumption was assessed using a single question where participants were asked on average how often they drank and to select a response from "daily or most days", once or twice a week", "once or twice a month", "once or twice a year," or "never". Responses were then dichotomised to weekly or more often versus less than weekly consumption (reference).

The dichotomies were selected to provide low/high alcohol consumption variables comparable across the two datasets.

Obesity

In NorStOP measures of self-reported body weight relative to self-reported height were used to calculate BMI by dividing weight in kilograms (kg) by the square of height in metres (m) (BMI = weight (kg)/[height(m)]^2). The collection of self-reported height and weight data has been found to be a valid and accurate method of measuring anthropometric characteristics in population studies (Spencer, Appleby, Davey, & Key, 2002) although the level of accuracy decreases in older populations (Kuczmarski, Kuczmarski, & Najjar, 2001). Responders were categorised into standard BMI groups. These are (i) underweight (BMI<18.5 kg/m^2), (ii) normal weight (BMI 18.5 – 24.9 kg/m^2),

(iii) overweight (BMI 25 –29.9 kg/m^2) and (iv) obese (BMI ≥30 kg/m^2) (World Health Organization, 2006). For the analysis undertaken in this study this variable was dichotomised into obese versus not obese (reference) as those meeting the criteria for obese are at greatest risk of health problems.

Sleep problems

Sleep problems were measured using the Jenkins Sleep Questionnaire (JSQ) (Jenkins et al., 1988). The questionnaire asks about recent problems with sleep and contains items on the most commonly occurring symptoms of poor sleep quality: sleep onset ('during the past four weeks did you have trouble falling asleep?'); sleep maintenance ('during the past four weeks did you wake up several times per night?'); early wakening ('during the past four weeks did you have trouble staying asleep, including waking up far too early?'); and non-restorative sleep ('during the past four weeks did you wake up after your usual amount of sleep feeling tired and worn out?'). Participants indicated the number of days in the past month that they have experienced difficulties in each of the four sleep components on a 3-point scale ranging; not at all/on some nights/on most nights. Sleep problems for each item were defined as problems experienced on most nights (Hayward, Jordan, & Croft, 2012); items were dichotomised into none/some versus most nights. Items were individually analysed because they represented different constructs of "difficulty with sleep initiation, duration, consolidation or quality" (American Academy of Sleep Medicine, 2005).

Health factors

Self-rated health

In ELSA participants were asked to indicate how they rated their health; 'excellent', 'very good', 'good', 'fair' or 'poor'. This variable was dichotomised to compare poor/fair ratings as the reference group to good, very good and excellent.

In the NorStOP dataset a measure of general health was used. General health was measured using a single item from the Medical Outcomes Study Short Form-12 (MOS-SF12) (Ware et al., 1995). In response to the need to produce a shorter instrument that could be completed more rapidly, the developers of the SF-36 produced the 12-item SF-12 using regression analysis. The selected 12 items reproduced 90% of the variance in the overall Physical and Mental Health components of the SF-36. The general health item required participants to rate their health as 'excellent', 'very good', 'good', 'fair' or 'poor'. This was dichotomised into poor/fair (reference) versus good/ very good/ excellent.
As before the dichotomies for the ELSA and NorStOP variables were determined to provide comparable variables across datasets comparing better to poorer self-rated health.

Functional limitation

In ELSA functional limitation was assessed using measurements of activities of daily living (ADL) (dressing, walking across a room, bathing or showering, eating, getting in or out of bed and using the toilet) and instrumental ADLs (IADLs) (map reading, preparing a hot meal, shopping for groceries, making telephone calls, taking medications, doing work around the house and garden and managing money). Participants scored 1 if they indicated difficulties with any of these activities and items were summed to form a scale

ranging from 0-13. An expanded scale measuring both ADL and IADL is unidimensional, has greater content validity for measuring the need for help and shows greater sensitivity to age (i.e. more accurately captures changes in functional health with age) than ADL measures alone (LaPlante, 2010). The combined scale also results in increased measurement equivalence between ELSA and a comparative national database, the Health and Retirement Survey (HRS) (Chan et al., 2012). Functional limitations were dichotomised around the median score (0) to produce categories of high and low limitation. This resulted in a comparison between no difficulties (reference) and any difficulties (24.57% of the study sample).

In NorStOP functional limitation was measured using the Medical Outcomes Study Short Form-36 which has been recommended for use in primary care research due to its brevity and extensive psychometric testing (Bohannon & DePasquale, 2010). The Physical Functioning Scale of the SF-36 has been used previously in other studies using NorStOP data as a measure of physical function/limitation (Jordan et al., 2012). This is a 10-item sub-scale, proposed as a measure of general physical activity (Ware & Sherbourne, 1992). The scores for the 10 items are summed and normalized so that total score ranges from 0-100, with higher scores indicating better physical functioning. Responders were empirically dichotomised according to whether or not their score lay below the median (reference) representing low physical function or above the median, representing high physical function.

Symptoms preventing walking

Participants were asked to specify what symptoms made it difficult for them to walk quarter of a mile. Options were chest pain, fatigue/too tired, shortness of breath, tremor, pain in leg or foot, swelling in leg or foot, incontinence, seeing difficulty, hearing difficulty, confusion, difficulty concentrating, memory problems, unsteady on feet or balance problems, lightheaded or dizziness, fear of falling, anxiety or fear or other problem or symptom. Variables were recoded and a single symptom count variable was created. This was again dichotomised around the median score to produce a category of high symptom count compared to a category of low symptom count. Using the median again resulted in a comparison between no difficulties (reference) and any difficulties.

Frailty

Using ELSA data, frailty was identified according to Fried's criteria (Fried et al., 2001). Physical measures taken as part of the nurse visit were used for weight loss, grip strength, and walking speed. Frailty was identified by the presence of three or more of the following characteristics: Weight loss (loss of ≥10% body weight since Wave 0 survey or BMI<18.5), low grip strength (in the lowest 20% of the distribution of scores, adjusted for age and sex, for maximum grip strength tested using a dynamometer), low walking speed (in the lowest 20% of the distribution for time taken to walk 8 feet at "usual" pace), low physical activity levels, (in the lowest sex specific 20% distribution for activity level (derived from the 3 questions about activity levels) and exhaustion (positive response to 2 CES-D questions ('felt everything was an effort' and 'could not get going' in the last week). Participants with less than three of these characteristics were categorised as the not frail group and formed the reference group in the mediation analysis. This approach to

identifying frailty has been used previously in the ELSA dataset (Gale, Baylis, Cooper, & Sayer, 2013) and is comparable to other studies using the clinical phenotype definition of frailty (Blyth et al., 2008; Gruenewald et al., 2009; Szanton et al., 2009).

Allostatic load

Determining allostatic load involves measurements of the activity of stress-regulatory systems (e.g., immune, cardiovascular, neuroendocrine, and metabolic) (Karlamangla, Singer, McEwen, Rowe, & Seeman, 2002). An estimate of allostatic load was derived in ELSA only using objective data collected by nurses including the information obtained from blood samples. The following measurements were used to create an allostatic load index (range 0-10): systolic blood pressure, diastolic blood pressure, mean arterial pressure, resting pulse rate, fibrinogen, high density lipid cholesterol (HDL), low density lipid cholesterol (LDL), C-reactive protein (CRP), glycosylated haemoglobin (HBA1C), and waist/hip ratio (Gruenewald et al., 2009; McEwen, 1998). Participants were allocated a score of 1 when their score was above the highest 25th percentile for nine of the measures and below the 75th percentile for HDL. Alternative criteria for calculating allostatic load have been examined such as summing the number of parameters for which an individual scored in the top (or bottom, according to highest risk) 10% of the distribution or averaging z-scores for each of the indicators however but the results were equivalent to using the quartile criteria (McEwen & Seeman, 1999). The allostatic load score was dichotomised around the median score for use in the mediation analyses. Scores ranged from 0-9 out of a possible 10, the median was 2 (IQR 1-4). Those scoring above the median (high allostatic load) were compared to those scoring below the median (low allostatic load) which formed the reference group.

Social factors

Social group membership

Group membership has been used as a measure of social participation in older adults in ELSA and was found to be an independent predictor of cardiovascular risk factors (Kamiya et al., 2010). Group membership was measured using eight items. Each participant reported current membership of or participation in (1) political party, trade union or environmental groups, (2) tenants groups, resident groups or neighbourhood watch, (3) church or other religious groups, (4) charitable associations, (5) education, art or music groups or evening classes, (6) social club, (7) sports club, gym or exercise classes or (8) any other organisations club or societies (Kamiya et al., 2010). The total score (0-8) was dichotomised at the median with membership of 0 or 1 group (reference) being compared to membership of 2 or more groups allowing low and high social group membership to be compared.

Volunteer work

In ELSA, participants were asked to indicate whether they undertook any voluntary work. This was dichotomised into 'yes' if they indicated any frequency of volunteer work and 'no' if they indicated they never did (Banks et al., 2014). This dichotomy of volunteer work has been used previously in ELSA and undertaking volunteer work was shown to be associated with increased quality of life in older adults (Netuveli, Wiggins, Hildon, Montgomery, & Blane, 2006), reduced depression and greater life satisfaction (McMunn Nazroo, Wahrendorf, Breeze, & Zaninotto, 2009).

Social participation

In NorStOP, social participation was measured using the Keele Assessment of Participation (KAP) (Wilkie et al., 2005) which measures taking part in 11 activities in accordance with the World Health Organization International Classification of Function (ICF) framework (World Health Organization, 2002) and include domains of mobility, domestic and major life (Wilkie et al., 2005) (Table AVII.1). Participants were considered to have reduced social participation if they reported that they were not taking part during the previous 4 weeks “as and when [they] wanted” for “some of the time” or less. The resulting 11 binary items were then summed to give a total score ranging from 0 to 11 and categorized to 0 (no restriction) and >=1 (any restriction) (Wilkie et al., 2005). The KAP has demonstrated adequate levels of reliability and validity for use in population studies (Wilkie et al., 2005).

Table AVII.1 Items from the Keele Assessment of Participation (KAP) (reproduced from Wilkie et al., 2005).
1. During the past 4 weeks, I have moved around in my home, as and when I have wanted. 2. During the past 4 weeks, I have moved around outside my home, as and when I have wanted. 3. During the past 4 weeks, my self-care needs (examples are washing, toileting, dressing, feeding, maintaining health) have been met, as and when I have wanted. 4. During the past 4 weeks, my home has been looked after, as and when I have wanted. 5. During the past 4 weeks, my things (belongings) have been looked after, as and when I have wanted. 6. Do you have any relatives, or other people, who depend on you? (Yes/No) If yes, during the past 4 weeks, were these people looked after, as and when you wanted? 7. During the past 4 weeks, I have met and spoken to other people as and when I have wanted. 8. During the past 4 weeks, I, or someone else on my behalf, have managed my money, as I have wanted. 9. Do you choose to take part in paid or voluntary work? (Yes/No) If yes, during the past 4 weeks, have you taken part in paid or voluntary work, as and when you have wanted? 10. Do you choose to take part in education or training courses? (Yes/No) If yes, during the past 4 weeks, have you taken part in education or training, as and when you have wanted? 11. Do you choose to take part in social activities? (Yes/No) If yes, during the past 4 weeks, have you taken part in social activities, as and when you have wanted

Psychological factors

Quality of life

In ELSA, quality of life was measured using the CASP-19 (Control, Autonomy, Self-realisiation and Pleasure) scale which was designed in a population of adults in early old age (65-75 years) (Hyde et al., 2003). CASP-19 has 19 items which map to four domains; control (4 items) for example 'I feel free to plan for the future', autonomy (5 items) for example 'I feel that I can please myself what I do', self-realisation (5 items) for example 'I feel that life is full of opportunities' and pleasure for example 'I enjoy the things that I do' (5 items). Responses options are 'often', 'sometimes', 'not often' and 'never' and are

scored 3-0 unless negatively worded where this is reversed. The psychometric properties (factor structure, content validity) of CASP-19 support its application in population studies and a test comparing the total model, a domain only model and a total and domain model demonstrated little difference between the latter two models indicating it is better to present the individual domain scores alongside the total quality of life score to give the scale greater utility (Sim, Bartlam, & Bernard, 2011). The enjoyment of life domain has previously been shown to be associated with longer survival in the ELSA dataset (Steptoe & Wardle, 2012). All quality of life domains were dichotomised at the median score for use in the mediation analysis to represent high (above the median) and low (below the median) quality of life specific to each domain (median scores were: Control = 9 (IQR 7-10), autonomy = 11 (IQR 9-13), self-realisation = 11 (IQR 8-13), pleasure = 14 (IQR 13-15), total = 44 (IQR 38-50)).

Anxiety and depression

In ELSA depression was measured using the eight item version of the 20 item Centre for Epidemiological Studies Depression (CES-D) scale. The CES-D is a short, structured self-report measure developed to assess depressive symptoms in epidemiological studies (Radloff, 1977). The reliability and factor structure of the 8 item scale has been tested and deemed to have internal consistency and be unidimensional (Gallo & Bradley, 2006; Steffick, 2000). Participants respond yes or no to eight questions regarding depressive symptoms (Table AVII.2). Responses were summed to give a score between 0 and 8 (two items worded in the positive direction were reverse scored) (Banks et al., 2014). The score was then dichotomised to no depression (score of 0 to 3) (reference) and possible case (score of 4 or more) (Steffick, 2000).

Table AVII.2 Items of the 8 item version of the CES-D (reproduced from Van de Velde, Levecque, & Bracke, 2009)
Much of the time during the past week…
…did you feel depressed?
…did you feel everything you did was an effort?
…was your sleep restless?
…were you happy?
…did you feel lonely?
…did you enjoy life?
…did you feel sad?
…were you unable to get going?

In NorStOP anxiety and depression were measured using the Hospital Anxiety and Depression scale (HADs) which was designed to detect the presence and severity of relatively mild mood disorders likely to be found in non-psychiatric hospital out-patients (Zigmond & Snaith, 1983). It was intended for use both as a screening device and to chart progress over time. It has been validated for use as a self-complete questionnaire. From a review of 747 studies which had used the HADs, overall the instrument performed well in identifying cases and assessing symptom severity of anxiety disorders and depression in somatic, psychiatric and primary care patients and in the general population (Bjelland et al., 2002). The scale comprises 14 items each with four response options (scored 0-3) which form two sub-scales (7 for anxiety and 7 for depression). Scores for each sub-scale are totalled across the 7 items with higher scores indicating greater anxiety or depression. The scores were calculated separately and categorised as non-cases (scores of 0-7), possible cases (8-10) and probable cases (11-21) (Zigmond & Snaith, 1983). For use in this study these items were dichotomised into non-cases versus possible/ probable cases.

Cognitive impairment

In ELSA cognitive impairment was measured using a memory test consisting of 10 words respondents were asked to recall immediately and five minutes later. The words were common nouns and were presented aurally by a computer. One word was presented every two seconds. Four different word lists were used interchangeably to ensure different versions of the test were administered to members of the same household (Llewellyn et al., 2008). The total number of words recalled (range 0-20) was used as an indication of memory (Banks et al., 2014). This was dichotomised around the median comparing a score of 0-10 (low cognitive ability) (reference) with 11-20 (high cognitive ability).

In NorStOP the 10-item Cognitive and Alertness Behaviour subscale from the Functional Limitations Profile (FLP) (the British version of the Sickness Impact Profile (SIP) was used to measure cognitive impairment (Table AVII.3). The SIP was designed to measure sickness related changes in normal life (Bergner et al., 1981), has previously been administered as a postal questionnaire (Trigg & Wood, 2003) and used as a measure of cognitive impairment in this dataset (Wilkie et al., 2007). Each item of the subscale has a simple yes/no response option, with responses being allocated a weight, and the summation of the 10 weights is then converted to a percentage value, with higher scores indicating poorer function. Scores of 0 formed the “no cognitive impairment” category (reference) and scores greater than 0 formed the impairment category where any cognitive impairment was indicated.

Table AVII.3 Items from the Cognitive and Alertness subscale (reproduced from McCracken & Iverson, 2001)
Forgetting a lot, recent things, appointments
Minor incidents
Not finishing things started
Not keeping attention on activity
Difficulty with concentration and thinking
Making mistakes
Difficulty reasoning and problem solving
Confusion
Reacting slowly
Behaving confused or disoriented

Perceived control over health

The Illness Perception Questionnaire (IPQ) (Weinman, Petrie, Moss-Morris, & Horne, 1996) was revised by Moss-Morris and colleagues in 2002 to enable a more accurate embodiment of the parallel-processing aspect of the SRM (described in Chapter One) and provides a tool to enable researchers to quantify people's illness perceptions and behaviours. The original questionnaire was improved and the scope of the existing subscales was extended for the cure/control and timeline components by creating separate subscales (Moss-Morris et al., 2002). The cure/control component was separated into personal control items and treatment control items. The timeline component was separated into acute/chronic items and cyclical items. Two further subscales were also added to incorporate emotional representations and to assess illness coherence.

In NorStOP a single item taken from the Revised Illness Perception Questionnaire at baseline (Moss-Morris et al., 2002) was used to measure personal control. Participants were asked to confirm 'yes' or 'no' to indicate their agreement to the statement 'there is a lot I can do to control my health' 'yes'/'no' (reference). There is a high correlation

between personal and treatment control items when the IPQ-R is used for musculoskeletal pain conditions as often patients are unlikely to have received much treatment so their representations of treatment effectiveness are indistinguishable from those of personal control (Nicholls, Hill, & Foster, 2013).

Appendix VIII - R code for mediation in survival analysis

```
library(foreign)

d<-read.dta("S:/Data/datasetname.dta")

d<-data.frame(d)

attach(d)

library(splines)

library(survival)


TE= coxph(Surv(time, censor) ~ pain + age + sex + education + income, data=d)

# view results

summary(TE)

mmediator=glm(mediator ~ pain + age + sex + education + income, family=binomial(), data=d)

# view results

summary(mmediator)

#for exponentiated estimates (ie ORs)  and 95%CI

exp(coef(mmediator))

exp(confint(mmediator))

doEffectDecomp=function(d)

{

# step1: replicate exposure variable, predict mediators

# ie logistic regression is used to get effect estimates for the influence of exposure on mediator

d$painTemp=d$pain

mmediator=glm(mediator ~painTemp + age + sex + education + income, family=binomial(),
data=d)


# step 2: replicate data with different exposures for mediator variable
```

ie dataframe is replicated with difference (counterfactual) values of exposure for mediator categories

d1=d2=d

d1$medmediator=d1$pain

d2$medmediator=!d2$pain

newd=rbind(d1, d2)

step 3: compute weights for mediator

newd$painTemp=newd$pain

w = predict(mmediator, newdata=newd, type='response')

direct = ifelse(newd$mediator, w, 1-w)

newd$painTemp=newd$medmediator

w=predict(mmediator, newdata=newd, type='response')

indirect=ifelse(newd$mediator, w, 1-w)

newd$Wmediator=indirect/direct

step 4: weighted Cox model

newd$W = newd$Wmediator

cox=coxph(Surv(time, censor) ~ pain + medmediator + age + sex + education + income, weight=W, data=newd)

return value: estimates of total, direct and indirect effects

TE=exp(sum(coef(cox)[c('pain', 'medmediator')]))

DE=exp(unname(coef(cox)['pain']))

IE=exp(sum(coef(cox)[c('medmediator')]))

#calculate proportion mediated

PM=log(IE)/log(TE)

return(c(exp(coef(cox)), TE=TE, DE=DE, IE=IE, PM=PM))

}

doEffectDecomp(d)

Step 5: get 95% confidence intervals for estimates obtained in step 4: step 4 doesn't produce confidence intervals so need to do bootstrap resampling

```
csamp=function(d)

{

s=sample(unique(d$surveyid),  replace=TRUE)

return(do.call('rbind', lapply(s, function(x) d[d$surveyid == x, ])))

}

HRs = replicate(100, doEffectDecomp(csamp(d)))

apply(HRs, 1, quantile, c(0.025, 0.975))
```

Appendix IX – Systematic review paper

OPEN ACCESS Freely available online

PLOS ONE

Chronic Pain and Mortality: A Systematic Review

Diane Smith[1]*, Ross Wilkie[1], Olalekan Uthman[2], Joanne L. Jordan[1], John McBeth[1]

1 Arthritis Research UK Primary Care Centre, Research Institute for Primary Care and Health Sciences, Keele University, Staffordshire, United Kingdom, 2 Warwick Centre for Applied Health Research and Delivery (WCAHRD), Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, United Kingdom

Abstract

Background: Chronic pain is common, often widespread and has a substantial impact on health and quality of life. The relationship between chronic pain and mortality is unclear. This systematic review aimed to identify and evaluate evidence for a relationship between chronic pain and mortality.

Methods: A search of ten electronic databases including EMBASE and MEDLINE was conducted in March 2012, and updated until March 2014. Observational studies investigating the association between chronic or widespread pain (including fibromyalgia) and mortality were included. Risk of bias was assessed and a meta-analysis was undertaken to quantify heterogeneity and pool results. A narrative review was undertaken to explore similarities and differences between the included studies.

Results: Ten studies were included in the review. Three reported significant associations between chronic or widespread pain and mortality in unadjusted results. In adjusted analyses, four studies reported a significant association. The remaining studies reported no statistically significant association. A meta-analysis showed statistically significant heterogeneity of results from studies using comparable outcome measures ($n=7$)($I^2=78.8\%$) and a modest but non-significant pooled estimate (MRR1.14,95%CI 0.95–1.37) for the relationship between chronic pain and all-cause mortality. This association was stronger when analysis was restricted to studies of widespread pain ($n=5$,$I^2=82.3\%$) MRR1.22(95%CI 0.93–1.60). The same pattern was observed with deaths from cancer and cardiovascular diseases. Heterogeneity is likely to be due to differences in study populations, follow-up time, pain phenotype, methods of analysis and use of confounding factors.

Conclusion: This review showed a mildly increased risk of death in people with chronic pain, particularly from cancer. However, the small number of studies and methodological differences prevented clear conclusions from being drawn. Consistently applied definitions of chronic pain and further investigation of the role of health, lifestyle, social and psychological factors in future studies will improve understanding of the relationship between chronic pain and mortality.

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* E-mail: d.smith48@keele.ac.uk

Introduction

Musculoskeletal pain is one of the most common complaints in adults [1]. It has a major impact on physical and mental health, daily activities and is a frequent reason for health care consultation [2–4]. Musculoskeletal pain may be associated with increased mortality although the relationship is unclear. Studies of single site pain (e.g. back pain [5,6]), hip and shoulder [7,8]) and simple counts of the number of pain sites [9,10] have produced conflicting results. A lack of consistency in case definitions of pain makes it difficult to compare studies and may explain some of the variation in findings.

Chronic pain may be a more useful starting point to examine the relationship between pain and mortality. There is potential for greater uniformity in case definition with use of recognised criteria [11]. Chronic pain, that is pain that lasts for three months or longer [11], is experienced by up to 30% of adults [12] and commonly occurs in multiple body sites [13]. Widespread pain, a sub-group of chronic pain and the cardinal symptom of fibromyalgia is linked with a greater impact than that of pain that is not widespread [3]. This review focusses on chronic pain, but additionally examined the relationship between chronic widespread pain and mortality. Chronic widespread pain is a phenotype that captures people with more severe pain that has a greater impact on outcomes [14,15]. We hypothesised that if chronic pain was associated with mortality that relationship would be strongest in those with chronic widespread pain.

To determine if chronic pain was associated with mortality, a systematic review was undertaken. The aims of the review were to identify and evaluate evidence to determine the strength of association between chronic pain and mortality, and in particular in the subgroup of studies investigating chronic widespread pain.

Methods

A protocol for the conduct of this systematic review and meta-analysis was developed with reference to Centre for Reviews and Dissemination (CRD) guidelines [16] and consisted of four phases: